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SPECIAL NOTICE

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The cover of this journal will be white enamel stock with title identification as the A. M. A. Archives of Neurology and Psychiatry in color, with date, volume and number also in color. The Table of Contents, which is now carried on the back cover, will be placed in the front of the journal directly preceding the lead article or editorial. Second, third and fourth covers will be used for color advertising.

Archives of Neurology and Psychiatry

VOLUME 64 SEPTEMBER 1950 NUMBER 3

ROLE OF SYMPATHETIC AND PARASYMPATHETIC SYSTEMS IN REFLEX DILATATION OF THE PUPIL

Pupillographic Studies

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THE ROLE of the sympathetic and parasympathetic mechanisms in the dilation reflexes of the pupil is still under discussion. Originally the cervical portion of the sympathetic chain was thought to be responsible for pupillary dilation; this belief was held until, back in 1861, Balogh [1] discovered that reflex dilation persisted after excision of the superior cervical ganglion. In 1878 C. R. Vulpian [2] observed reflex dilation after removal of both the upper cervical and the stellate ganglion; he concluded that this dilation was mediated by sympathetic dilator fibers outside the cervical sympathetic chain. In 1883 von Bechterew [3] suggested that pupillary dilation to pain stimuli might be caused by inhibition of the third nerve, rather than by impulses running over the peripheral sympathetic fibers. Braunstein [4] expressed himself in favor of Bechterew's hypothesis, since, after having cut the third nerve intracranially, he could no longer obtain reflex dilation to pathic stimulation twelve days to seven months after the operation. In contrast

This work was aided by grants from the Harriman Fund and the Duntery Milbank Foundation.

From the Department of Ophthalmology (Laboratory of Pupillography), Columbia University College of Physicians and Surgeons, and the Institute of Ophthalmology, Presbyterian Hospital.

1. Balogh: Moleschotts Untersuchungen, Heidelberg, Carl Winter, 1861, vol. 8, p. 423.

2. Vulpian, A.: Note relative à l'influence de l'extirpation du ganglion cervical supérieur sur les mouvements de l'iris, normal et pathologique, Arch. Physiol. **1**:177, 1874; cited by Vulpian, C. R.: Expérience démontrant que les fibres nerveux, dont l'excitation provoque la dilatation de la pupille, ne proviennent pas toutes du cordon cervical du grand sympathique, ibid. **86**:1436-1437, 1878.

3. von Bechterew, A.: Ueber den Verlauf der die Pupille verengernden Nervenfasern im Gehirn und über die Localisation eines Zentrums für die Iris und Contraction der Augenmuskeln, Arch. f. d. ges. Physiol. **31**:60-87, 1883.

4. Braunstein, E. P.: Die Lehre von der Innervation der Pupillenbewegung, Wiesbaden, J. F. Bergmann, 1894.

to these findings, Anderson [5] observed in experiments on cats that after section of the third nerve dilation of the pupil may readily be produced by tactile and pathic stimuli; the dilation, however, ceased when the cervical sympathetic fibers were also cut.

The more recent literature, as represented by the publications of Ury and Gellhorn,[6] Ury and Oldberg [7] and Seybold and Moore,[8] is in favor of parasympathetic inhibition as the main factor in reflex dilation of the pupil and considers sympathetic active dilation a negligible factor. Ury and Gellhorn concluded (*a*) that the difference in dilation between the normal and the sympathectomized pupil, in response to stimulation of the afferent nerves, is largely due to the tonic action of the sympathetic fibers, and (*b*) that reflex excitation of the sympathetic fibers plays at most an insignificant role.[9] Ury and Oldberg went further when they stated that reflex dilation of the pupil is "mediated solely by central inhibition of the Edinger-Westphal nucleus" [10] and that "none of the variability of the pupil to light or afferent stimuli is lost when the sympathetic component is interrupted, but the magnitude of the reaction is diminished." [11]

Ury and Gellhorn, Ury and Oldberg and Seybold and Moore sectioned the third nerve of cats intracranially. Ury and Gellhorn stated:

> . . . Since the pupil, after division of the third nerve, is wide if not maximally dilated, it is unsuited for the study of sympathetic action, but 1 to 2 drops of a 1 per cent eserine solution applied locally cause a constriction of the iris and permits the study of reflex dilatation.[12]

They claimed: [12]

> . . . The threshold of the pupillo-dilator fibers in the cephalad end of the divided cervical sympathetic is . . . not altered by eserine [and that, therefore,] a dilatation of the eserinized and parasympathectomized eye following a peripheral stimulus indicates sympathetic excitation; absence of such dilatation, when the normal eye dilates, indicates that the action is exclusively through inhibition of the tonus of the third nerve.

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5. Anderson, H. K.: Reflex Pupil Dilatation by Way of the Cervical Sympathetic Nerve, J. Physiol. **30**:15-24, 1904.

6. Ury, B., and Gellhorn, E.: Rôle of the Sympathetic System in Reflex Dilatation of Pupil, J. Neurophysiol. **2**:268-275, 1939.

7. Ury, B., and Oldberg, E.: Effect of Cortical Lesions on Affective Pupillary Reactions, J. Neurophysiol. **3**:201-212, 1940.

8. Seybold, W. D., and Moore, R. M.: Oculomotor Nerve and Reflex Dilatation of Pupil, J. Neurophysiol. **3**:436-441, 1940.

9. Ury and Gellhorn,[6] p. 271.

10. Ury and Oldberg,[7] p. 202.

11. Ury and Oldberg,[7] p. 208.

12. Ury and Gellhorn,[6] p. 268.

Kuntz and Richins,[13] also working on cats, found that "in the intact animals, direct stimulation of the cervical sympathetic trunk elicited maximal dilatation of the pupil on the same side." Parasympathetic denervation of the eye resulted in marked enlargement of the homolateral pupil but not in its maximal dilation. Additional stimulation of the cervical part of the sympathetic trunk resulted in further dilation of the parasympathectomized pupil—from 10.2 to 14.5 mm. They therefore concluded:

> Maximal pupillary dilatation probably requires active contraction of the radial muscle of the iris which is innervated through sympathetic nerves. Peripheral pain producing stimulation elicits moderate reflex dilatation of the pupil; this reaction is not altered by sympathetic denervation of the eye but is abolished by section of the oculomotor nerve or extirpation of the ciliary ganglion; consequently, it is mediated through the parasympathetic nerves.[14]

But since the reflex pupillodilator response elicited by peripheral stimulation was greatly reduced after incomplete depression of the adrenergic nerves by the intravenous administration of ergotoxine, the authors assumed that the pupillodilator reaction is mediated through the parasympathetic center in the mesencephalon and that the pupillodilator reaction is actively integrated and controlled. This active inhibition of the sphincter pupillae "is brought about, not by inhibition of the parasympathetic center, but by activation of this center which results in the discharge of efferent nerve impulses through the adrenergic fibers arising in the ciliary ganglion."

Ward and Reed[15] stimulated the lateral and medial surfaces of the frontal lobe in monkeys (Macaca mulatta). They found that electrical stimulation of the frontal cortex around the anterior tip of the superior limb of the arcuate sulcus yielded consistent bilateral pupillary dilation. Unilateral cervical sympathectomy abolished the pupillary dilation in the sympathectomized eye on cortical stimulation of either hemisphere, a maximal dilation in the normal eye being still elicitable. With the animal under light ether anesthesia, a minimal pupillary dilation of 0.5 to 1 mm. in the sympathectomized eye could be obtained on cortical stimulation, as compared with a dilation of 4 mm. in the normal eye. Section of the third nerve intracranially with the peripheral sympathetic fibers unimpaired caused the pupil to dilate to 7 mm. Subsequent cortical stimulation continued to produce prompt dilation of both pupils, the parasympathectomized pupil then dilating from 7 to 10 mm., while the normal pupil continued to dilate from 3 to 9 mm. Subsequent

13. Kuntz, A., and Richins, C. A.: Reflex Pupillodilator Mechanisms: An Experimental Analysis, J. Neurophysiol. **9**:1-7, 1946.

14. Kuntz and Richins,[13] p. 6.

15. Ward, A. A., Jr., and Reed, H. L.: Mechanism of Pupillary Dilatation Elicited by Cortical Stimulation, J. Neurophysiol. **9**:329-335, 1946.

unilateral cervical sympathectomy on the same side abolished all pupillary dilation in the previously parasympathectomized pupil. The authors concluded that (1) the active component of pupillary dilation elicited by cortical stimulation travels over the sympathetic system; (2) the third nerve is not a necessary component of the pupillodilator response elicited by cortical stimulation; (3) in active pupillary dilation elicited by cortical stimulation, a minimal inhibiton of parasympathetic tone is produced of the same order as that which obtains in reciprocal innervation elsewhere in the nervous system. In order to find the pathways over which these effects were mediated, Ward and Reed strychninized the cortical tip of the arcuate sulcus, while a bipolar recording electrode was placed in the oculomotor nucleus. Strychninization resulted in typical firing in the oculomotor nucleus. The area from which firing was obtained corresponded very closely with area 8. A direct projection from area 8 to the oculomotor nucleus was demonstrated, and the authors concluded that the minimal inhibition of activity in the oculomotor nucleus obtained by cortical stimulation is transmitted over this pathway. Since in unilaterally sympathectomized monkeys hypothalamic stimulation caused prompt maximal dilation in the normal pupil alone, it was concluded that the lateral hypothalamus approximates the final common path of the active components of pupillary dilation and is not concerned with the reciprocal inhibition of the oculomotor nucleus which has been elicited from area 8 of the cortex. That multiple strychninization of the frontal cortex, including area 8, failed to fire into the hypothalamic region indicates that if the lateral hypothalamus is involved in the pathway between cortex and sympathetic chain, as shown by Hodges and Magoun, there must be more than one synapse between the cortex and it. Electrical stimulation of the lateral hypothalamus yields pupillary dilation without inhibition of the oculomotor nucleus. The authors therefore concluded that pupillary dilation elicited by electrical stimulation of area 8 of the cerebral cortex of the monkey is a localized sympathetic response having all the properties of reciproval innervation.

Weinstein and Bender [16] compared pupillary dilation reflex activity in cats and in monkeys. In agreement with Ury and Gellhorn, Ury and Oldberg and Seybold and Moore, they found that in cats dilation was not abolished after section of the cervical sympathetic trunk but was no longer seen after section of the oculomotor nerve.[17] In contrast,

16. Weinstein, E. A., and Bender, M. B.: Pupillodilator Reactions to Sciatic and Diencephalic Stimulation: A Comparative Study in Cat and Monkey, J. Neurophysiol. **4**:44-50, 1941.

17. In reading their experimental data [16] (page 48), however, it can be seen that, although at 12:47 p. m. the left third nerve was transected, pupillary dilation of 1.5 mm. on the same side was described on stimulation at A-11 R_3 H-6 (border of the ventromedian hypothalamic nucleus).

they found the reflex pupillary dilation in monkeys abolished or greatly reduced by cutting of the cervical sympathetic trunk but present after section of the third cranial nerve.

In pupillographic experiments on man made for clinical purposes, we consistently found that impairment of the peripheral sympathetic fibers, within the third neuron, reduced or eliminated the reflex dilation to sensory or emotional stimuli, whereas we frequently observed normal reflex dilation in cases of impaired light reflex when this impairment was due to a lesion of the third nerve. Pupillographic studies on 9 monkeys with various lesions in the cervical sympathetic trunk or the third nerve gave results similar to those in man.

In view of the great and unreconcilable discrepancies in the literature and our own clinical experiences in man and experimental findings in monkeys, we considered it necessary to carry out systematic studies in which errors of observation were eliminated by pupillographic recording.

These experiments were performed on cats.

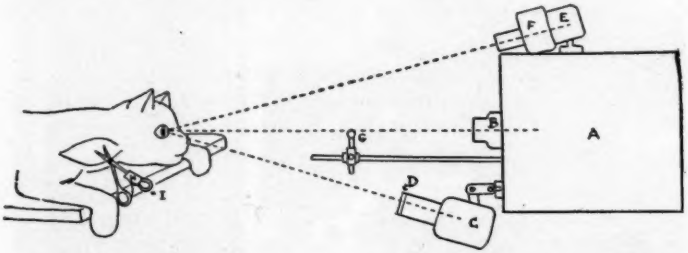

Fig. 1.—Schematic drawing showing experimental setup for pupillography. *A* indicates pupillographic camera; *B*, lens of pupillographic camera; *C*, source of red-infra-red light; *D*, Wratten no. 88A red-infra-red filter; *E*, source of light for stimulation; *F*, interrupter mechanism for timing of light stimulus; *G*, signal light; *H*, microswitch, and *I*, cutting scissors.

METHODS

We used 38 cats in which we had, at some time prior to the experiment, removed the nictitating membrane to avoid its interference with pupillographic recording. In one series, of 6 cats, recording was done while the sympathetic nerve was sectioned, either preganglionically or postganglionically, and was continued after the section, until anisocoria was fully developed. With the animal under ether anesthesia, the sympathetic nerve fibers (preganglionic or postganglionic) were isolated and slipped onto the cutting scissors. An electric microswitch (fig. 1, *H*), operating a signal light (fig. 1, *G*), was fastened to the scissors (fig. 1, *I*) in such a way that it turned on the light at the moment the scissors were closed. The signal was recorded on the film. It is evident that this method of indicating the moment of cutting is not of high precision, for, depending on the position of the nerve fibers on the scissors, the moment of sectioning and the moment of the light signal may not be quite identical. Therefore, latency periods of the immediate reaction to the section were not determined. In some cases the signal light was used merely to indicate the moment of cutting;

in others it was placed before the cat's eye, thus eliciting a light reflex at the very moment of sectioning and/or at any chosen moment thereafter. With the sympathetic nerve fibers exposed, the cat was carefully placed in front of the pupillographic equipment (fig. 1). As soon as the cat was in the proper position, administration of ether was discontinued, and sufficient time was allowed to elapse until anesthesia became light enough that the cat might be expected to awake within the next four minutes. At this moment the recording was started, and after about five seconds the nerve was cut. Pupillographic recording was continued until the animal awoke, or, as in 1 case, died.

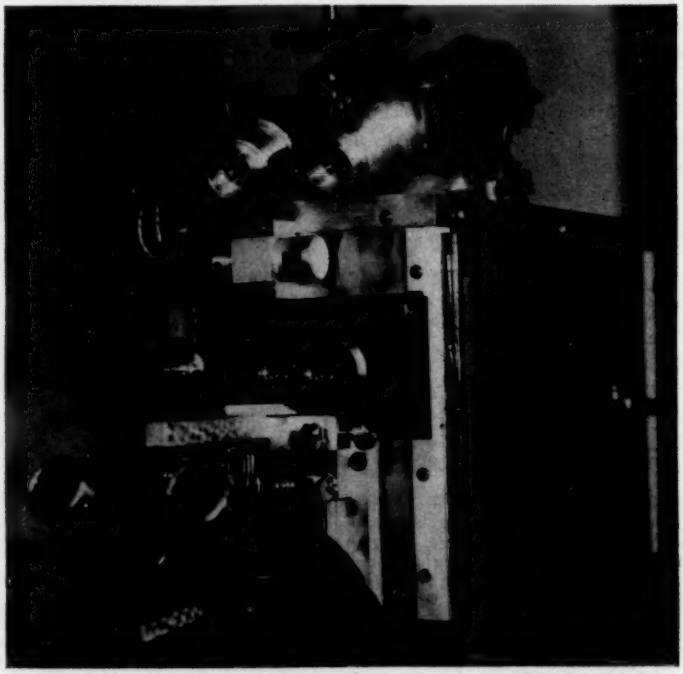

Fig. 2.—Photograph of pupillographic equipment.

In another series of experiments, pupillary movements following sensory stimuli, particularly sound and pain stimuli, were recorded, both in normal and in sympathectomized and parasympathectomized cats, from forty-eight hours to two months after the operation. In these experiments 30 cats were used and about 500 psychosensory reactions recorded pupillographically; the animals were awake and not under the influence of any drugs. Special equipment was used to keep the animal in place. It did not allow much movement but was elastic enough not to hurt or otherwise irritate the cat. A kind of "psychologic" treatment of the animal is necessary in such experiments, which were begun only when the animal was adapted to the conditions. When, nevertheless, the animal started to struggle, we patiently waited until it again calmed down. Some animals adapted easily

and seemed to like being handled in this way, purring throughout the experiment. A few cats, in spite of all efforts, proved to be unadaptable and were discarded.

While the experiments were going on, the laboratory and its surroundings had to be quiet; if we could not reach this goal during the daytime, we made our experiments at night.

The experiments themselves were performed under the condition of darkness. The pictures were taken under dark red–infra-red illumination on 35 mm. Kodak® spectroscopic film (type 1-N), running at a speed of 10 frames per second. The infra-red light was obtained by using the Wratten filter no. 88-A in front of a tungsten source (fig. 1, *C* and *D*).

The pupillographic instrument enabled us, by means of a mechanically geared timing device (fig. 1, *F*), to throw light stimuli of a well defined intensity and duration at chosen intervals centrally into either the right or the left eye of the cat. As the intensity of the light stimuli we chose 15 foot candles; as the duration, one second, and as dark intervals between the light stimuli, three seconds. More than 500 light reflexes were recorded pupillographically.

In order to stimulate the animal emotionally, we used sensory stimuli, such as a short period of blowing into the face of the cat, a sound (pistol shot), a painful stimulus (pinprick) or the imitation of a barking dog, at a certain well defined moment within the dark interval between light stimuli.

To obtain the pupillographic curves from the series of images on the motion picture film, the sizes of the pupils were measured. The film was projected onto a screen, and measurement was made by means of a measuring compass at an enlargement of 30 diameters. Since the cat's pupil is not circular, but a more or less dilated slit, we measured the largest diameter at right angles to the longitudinal axis of the slit (fig. 3). This diameter was plotted as the ordinate against time, in terms 0.1 second, as the abscissa. The resulting curve, the pupillogram, shows the constantly changing pupillary diameter.

Study of this pupillogram was made with the aid of differential analysis, resulting in a differential curve. The differential curve was obtained by measuring the extent of contraction (in terms of 0.01 mm.) within each successive tenth of a second and by plotting the values obtained as the ordinate, against time (in terms of 0.1 second) as the abscissa.

RESULTS

1. *Development of Anisocoria.*—When the sympathetic nerve is cut, the immediate reaction is a dilation of the homolateral pupil.

Figure 4 shows a typical reaction in a case of postganglionic sympathectomy. The animal was under light ether anesthesia. Before the nerve was cut on the right side, the diameter of the right pupil (7.9 mm.) was smaller than that of the untouched, left pupil (10.1 mm.). This anisocoria was observed to develop during the operation preceding section and was doubtless due to the trauma of handling the nerve during operation. It was observed in 4 of 5 cases.

The immediate reaction to section of the nerve, namely, dilation of the pupil, was strictly homolateral. The nonsympathectomized pupil did not show any reaction. The dilation amounted to 2.2 mm. in 1.2 seconds and did not occur at an even speed. Figure 5 shows the increase

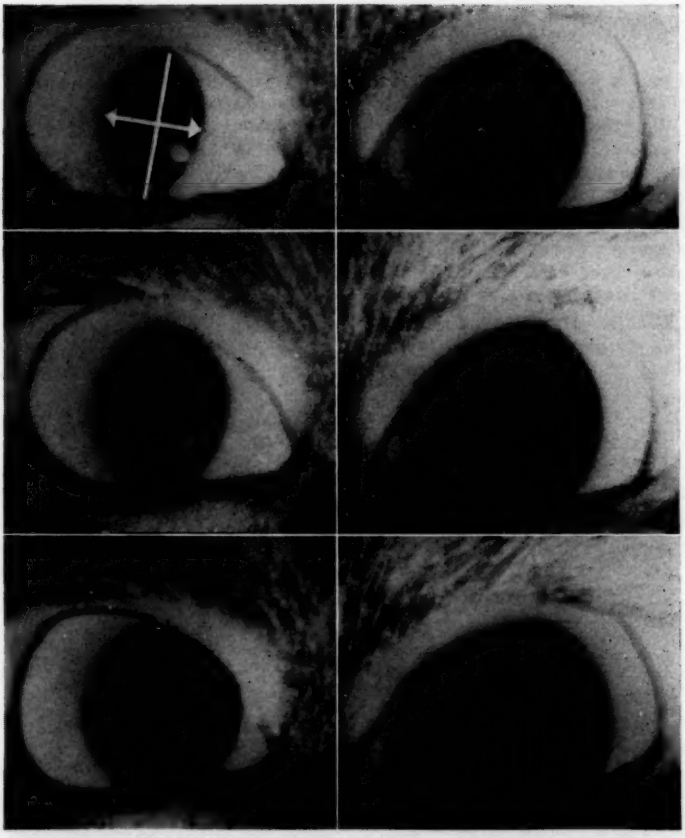

Fig. 3.—Pictures obtained from the pupillographic film of a cat. The widest diameter at right angles to the longitudinal axis of the pupil (as indicated by arrow) was measured.

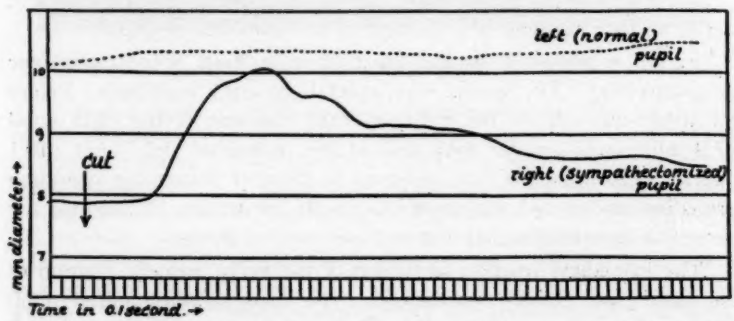

Fig. 4.—Pupillographic records of both pupils during section of the cervical sympathetic trunk.

Before section of the right cervical sympathetic trunk, anisocoria existed (right pupil, 7.9 mm.; left pupil, 10.1 mm.); after section the right pupil dilated and recontracted, and the left pupil was unaffected.

and decrease in speed of dilation. The ordinate represents the amount, expressed in millimeters, of dilation within each successive tenth of a second. The abscissa represents time, in terms of 0.1 second. The curve shows that the maximum speed was reached 0.3 second after the beginning of the dilation and amounted to 0.8 mm. within 0.1 second, i. e., 8 mm. per second. This maximal speed was maintained for only 0.1 second and was followed by a gradual decline in speed of dilation.

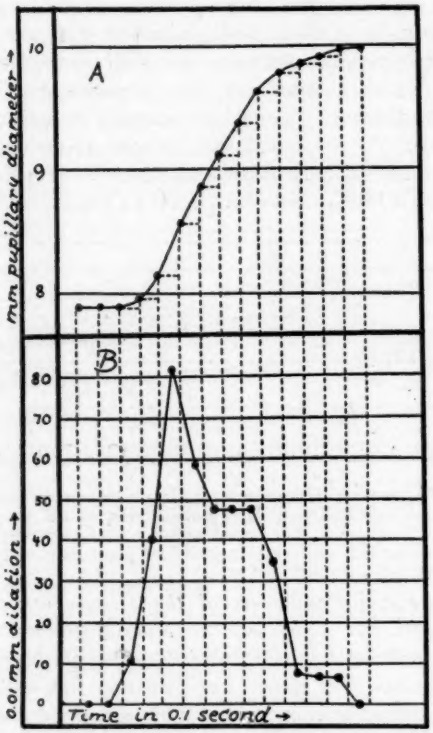

Fig. 5.—*A*, pupillographic record of a dilation resulting from section of the peripheral postganglionic sympathetic fibers. The ordinate represents the pupillary diameter, in millimeters; the abscissa represents time, in intervals of 0.1 second.

B, differential curve showing the increase and decrease in speed of dilation of the curve shown in *A*. The ordinate represents pupillary dilation, in 0.01 mm., within each successive tenth of a second; the abscissa represents time, in 0.1 second.

When the dilation came to an end, it was followed by a relatively, and increasingly, slow recontraction. In all our curves we found this contraction to occur in waves rather than in one even motion (fig. 4). About six seconds after dilation started, the pupil again reached the

diameter it had before the nerve was cut. Beyond this point the contraction continued, at a very slow rate, until after about ninety seconds anisocoria reached its maximum of 3.5 mm.

While the curve shown in figure 4 is typical so far as the general outline of the movements described is concerned, the dimensions of the movements differ in individual cases.

The experiment itself is of basic importance. It shows that the shape of a localized unilateral sympathetic reaction, such as that produced, under the condition of general anesthesia, by section of a sympathetic nerve, is in all its details identical with that of generalized and bilateral movements which, as we shall show later, follow (1) sensory stimuli, such as touch or pain, somewhere at the periphery, for instance, the skin; (2) visual and acoustic stimuli, causing fear or other emotion, or (3) the spontaneous or pseudospontaneous course of the contents of the animal's consciousness, without preceding sensory stimulation, which lead to emotions, such as rage.

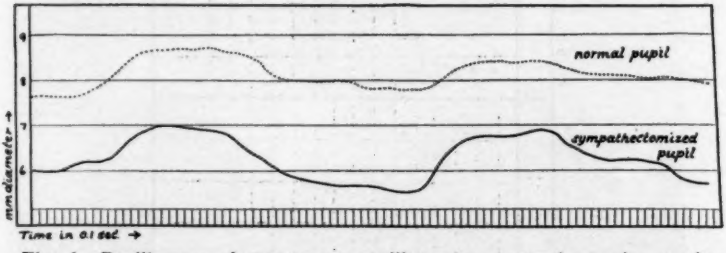

Fig. 6.—Pupillogram of spontaneous pupillary movements three minutes after unilateral cervical sympathectomy. The animal was on the verge of awakening from light ether anesthesia. The spontaneous contractions and dilations were slightly more pronouncd in the sympathectomized pupil than in the normal pupil.

2. *Divergence and Parallelism of the Movements of the Sympathectomized Pupil and Those of the Normal Pupil.*—As we stated previously, the reaction following section of the peripheral sympathetic nerve fibers consists of a rather rapid dilation followed by a gradual and unsteadily declining contraction. This movement, we emphasized, is restricted to the homolateral pupil. When we observed the pupils with the unaided eye, it sometimes seemed that both pupils dilated. Pupillographic recordings show that indeed, at times, both pupils dilate. However, this type of movement is different from that previously described as the effect of cutting the sympathetic fibers.

Figure 6 shows such movements. After preganglionic sympathectomy, anesthesia had become very light, and the animal was on the verge of awakening. The contractions and dilations resulting from impulses on awakening were slightly more pronounced in the pupil which had been sympathectomized three minutes before.

Since the dilation of the sympathectomized pupil cannot be due to impulses running over the peripheral sympathetic nerves, it must be due to activity of the third nerve. The fact that dilation is fully preserved on the sympathectomized side seems to indicate that it is due entirely to relaxation or inhibition of the third nerve.

The phenomenon in the cat's sympathectomized pupil of spontaneous dilations which are parallel with, and usually even slightly stronger than, those of the nonsympathectomized pupil appeared time and again in our experiments. This seemingly paradoxic behavior can be explained on the assumption that the sympathetic system is an inhibitor of the parasympathetic system. When the sympathetic nerve supply is removed, the parasympathetic fibers are disinhibited in all their functions, both those leading to contraction (activity) and those leading to dilation (relaxation).

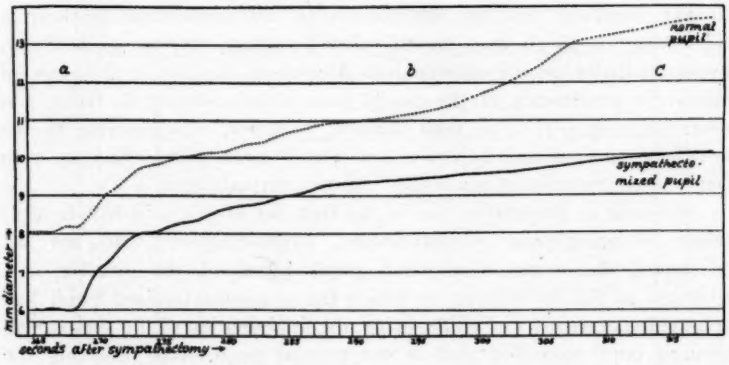

Fig. 7.—Pupillary dilation preceding the moment of death, 265 seconds after unilateral cervical sympathectomy.

(*a-b*) Dilation of both pupils. Dilation of the sympathectomized pupil was slightly greater than that of the normal pupil.

(*b-c*) Final pupillary dilation just before death. The normal pupil dilated four times as much as the sympathectomized pupil.

3. *Role of the Peripheral Sympathetic Fibers at the Moment of Death.*—We recorded the movements of the pupils in death, which occurred 225 seconds after sympathectomy (fig. 7). Until 190 seconds after section of the peripheral (postganglionic) sympathetic fibers the experiment took an uneventful course. At this moment the two pupils simultaneously began to contract—the left pupil 4.5 mm., and the right pupil 3.5 mm., within 50 seconds, i. e., at a rate of 0.09 and 0.07 mm. per second, respectively. They remained contracted for about 20 seconds and then suddenly redilated. This dilation (fig. 7, *a* to *b*) remained almost equal on the two sides and showed movements of the same shape.

It lasted 25 seconds and amounted to about 3.5 mm. on each side, i. e., 0.13 mm. per second. From this moment, the dilation of the sympathectomized pupil had come virtually to an end. Within the next 20 seconds it dilated only an additional 0.6 mm. (fig. 7, *b* to *c*), at an average speed of 0.03 mm. per second. In contrast, the dilation of the normal pupil accelerated. It amounted to 2.4 mm. within the same 20 seconds (average speed, 0.12 mm. per second) and resulted in nearly maximal enlargement of the normal pupil. This observation shows that the dilations of the two pupils (up to *b* of fig. 7) preceding death were homologous movements, almost equal in rate, shape and dimension on the two sides, but slightly more pronounced on the sympathectomized side, and therefore due to inhibition or relaxation of the third nerve. At the moment of death, however, the normal pupil showed (fig. 7, *b* to *c*) 1.8 mm. more dilation than the sympathectomized one. This difference must be due to sympathetic activity.

We observed pupillary movements at the moment of death in a second cat in which, two months after postganglionic sympathectomy, hypersensitivity to epinephrine had developed. Up to the moment of death the movements of the pupils were closely similar to those just described (fig. 7). The final dilation, however, was extreme in the sympathectomized and hypersensitive pupil, causing it to become even larger than the almost maximally dilated normal pupil.

We wish to emphasize that in the first cat (fig. 7), in which, after recent postganglionic sympathectomy, hypersensitivity had not yet developed, the sympathectomized pupil remained the smaller one, whereas, in the second cat, in which the sympathectomized pupil had become hypersensitive to epinephrine, the final dilation of the sympathectomized pupil exceeded that of the normal pupil, thus reversing the anisocoria.

4. *Influence of the Sympathetic Fibers on the Pupillary Reflex to Light.*—Pupillary reflexes to light were elicited (1) immediately after the moment of section and (2) five minutes later.

Figure 8 *A* shows an experiment in which, less than one second after the preganglionic sympathetic nerve fibers were cut, a light reflex was elicited in the sympathectomized eye. Both the direct reaction of the sympathectomized pupil and the consensual reaction of the normal pupil were present. The sympathectomized pupil in this case of preganglionic sympathectomy was larger than the normal pupil (sympathectomized pupil, 12.9 mm.; normal pupil, 12.3 mm.). The light reflex was elicited at the moment when the immediate dilation in response to section had come to an end and the pupil was ready to contract. Therefore, we could not find a latency period on the sympathectomized side, whereas the consensually reacting normal pupil showed the normal latency period. Both pupils contracted (*a* to *b*) and

redilated (*b* to *d*). The contraction to light of the sympathectomized pupil was more extensive than that of the normal one (2.3 and 1.6 mm., respectively). Redilation occurred in two phases. The first phase (*b* to *c*) was equal on the two sides; the second redilation phase (*c* to *d*) was well developed on the normal side (1.3 mm.) but was greatly reduced on the sympathectomized side. At *d* the tendency to contraction due to sympathectomy became more powerful than any possible tendency to dilation, and the pupil resumed its contraction.

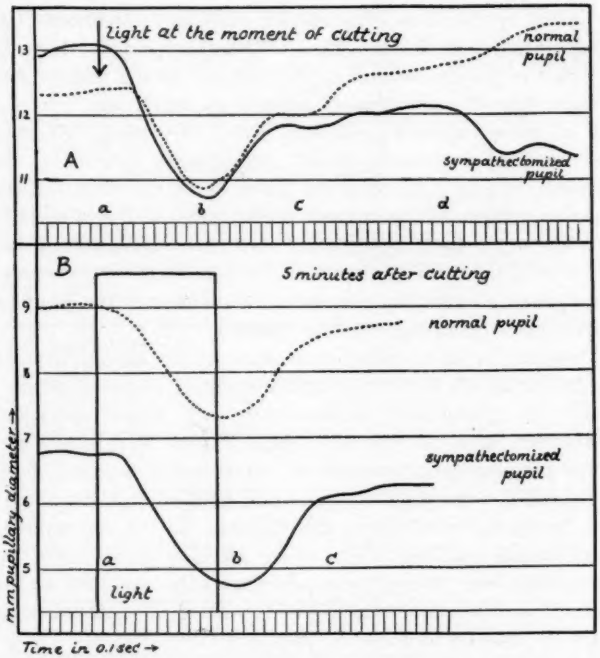

Fig. 8.—*A*, light reflex elicited immediately after unilateral section of the cervical sympathetic trunk.

(*a-b*) Contraction of both pupils. The contraction was greater on the sympathectomized side.

(*b-c*) Primary redilation phase. The two pupils redilated equally.

(*c-d*) Secondary redilation phase; the dilation was well developed on the normal side but was almost absent on the sympathectomized side.

B, light reflex elicited five minutes after unilateral cervical sympathectomy. Both contraction (*a-b*) and primary redilation (*b-c*) were slightly greater on the sympathectomized side than on the normal side.

Figure 8, line 2, shows the effect of a light stimulus five minutes after sympathectomy; although the sympathectomized pupil had become 2.25 mm. smaller than the normal one, its contraction to light was

slightly more pronounced than that of the normal pupil (2 and 1.73 mm., respectively).

These experiments illustrate what we have found in all similar experiments; that is, (1) cervical sympathectomy facilitates the contraction to light; (2) the first phase of redilation following contraction to light is not impaired by sympathectomy and therefore must be due entirely to relaxation or inhibition of the third nerve; (3) the second redilation phase is almost absent in sympathectomized eyes and therefore must depend on the peripheral sympathetic fibers being unimpaired.

5. *Effect of Sensory Stimuli on Pupillary Dilation.*—Cats are extremely sensitive to sensory stimuli. Whether or not differences exist in the effect of painful stimuli to the skin, or to the sciatic or another nerve, and that of such sensory stimuli as sound was not made the subject of more extensive research work. A cursory glance at our material does not seem to reveal any characteristic differences.

However, it was noted that the intensity of the stimulus, the basic emotional condition of the animal at the time of the stimulation and the intensity of the basic illumination determined the extent of reaction; in other words, the initial diameter as the expression of the sympathetic-parasympathetic equilibrium present at the moment of the psychosensory stimulation determined the extent of dilation.

In studying the effect of psychosensory stimuli on pupillary dilation, we had to distinguish between sympathectomized pupils in which hypersensitivity to epinephrine existed and such pupils in which this hypersensitivity had not yet developed. Figure 9*A* shows a case in which the preganglionic sympathetic nerve supply was cut forty-eight hours before; the reactions to sound and pain stimuli amounted to 1.0 mm. on the normal side but to only 0.2 mm. on the sympathectomized side; this means that four fifths of the effect was conducted over the cervical sympathetic nerve fibers and that only one fifth was due to inhibition of parasympathetic activity. No difference was found between responses to sound and those to pain.

Figure 9*B* shows a variation of this experiment. In figure 9*A* psychodilation was produced by sound and pain stimuli after the pupils had adapted to dark red–infra-red illumination and the pupillary diameters amounted to 7.0 and 7.5 mm., respectively, on the normal side, and to 4.8 to 4.3 mm. on the sympathectomized side. In figure 9*B*, after adaptation to dark red–infra-red light, the normal pupil measured 8.0 mm. and the sympathectomized pupil 7.0 mm. Before the sound stimulus was applied, the pupils were contracted by four successive light stimuli (of one second's duration each at intervals of two seconds); at the moment of the sound stimulus they had a diameter of 4.3 mm. on the normal side and of 2.1 mm. on the sympathectomized side. Under these conditions, psychosensory dilation was far more extensive than

in the experiment of figure 9 *A*, namely, 4.5 mm. on the normal side and 1.5 mm. on the sympathectomized side. However, in spite of the greater extent of the reaction, the sympathectomized pupil still dilated only 20 per cent of the simultaneous normal reaction. We conclude, therefore, that four fifths of the active reflex dilation is conducted over

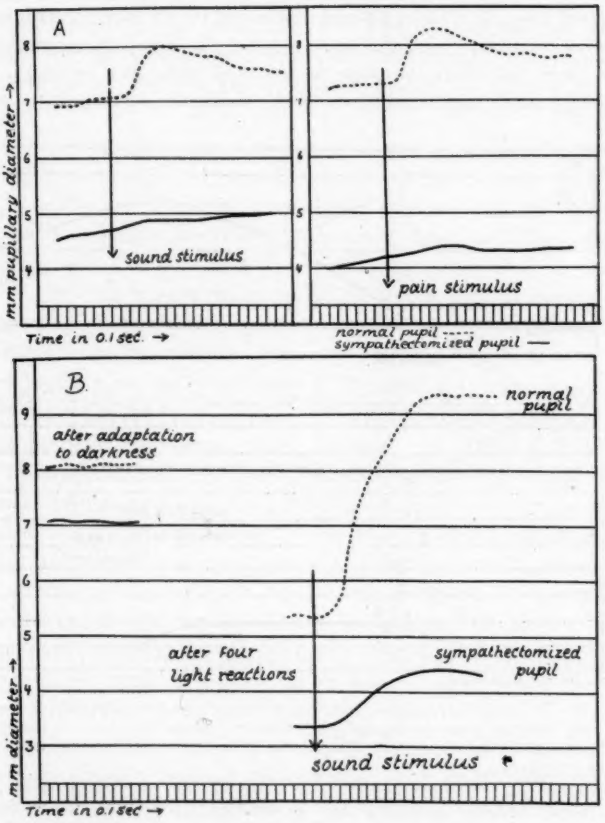

Fig. 9.—Pupillary dilation in response to sensory stimuli after unilateral peripheral sympathectomy.

(*A*) Both pupils were adapted to dark red-infra-red light; both the sound stimulus and the pain stimulus caused both pupils to dilate, the normal pupil more than the sympathectomized one.

(*B*) The pupils were contracted by four successive light stimuli to the normal pupil; a sound stimulus caused both pupils to dilate, the normal pupil more than the sympathectomized one.

the peripheral sympathetic nerve fibers and only one fifth over the pathways of so-called central sympathetic inhibition.

Figure 10 shows a case in which, two months after cervical postganglionic sympathectomy, hypersensitivity to epinephrine had developed. The anisocoria present was only minor (sympathectomized pupil, 6.9 mm.; normal pupil, 7.1 mm.). When a sound stimulus was produced, the right pupil, after a latency period of 0.2 second, dilated in the characteristic, rather abrupt movement. This response lasted 0.3 second (fig. 10 *A*, *a* to *b*) and amounted to 1.5 mm. (average speed, 5 mm. per second). In the same period the sympathectomized pupil dilated only 0.2 mm. (average speed, 0.67 mm. per second). After the normal pupil had reached its peak of dilation, it began to contract

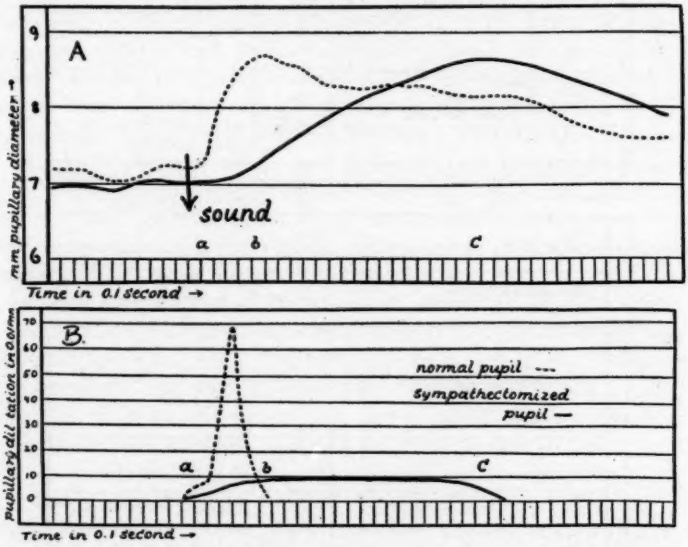

Fig. 10.—*A*, pupillary dilation in response to a sound stimulus in a cat in which, two months after postganglionic cervical sympathectomy, hypersensitivity to epinephrine had developed. *B*, differential curve showing increase and decrease in speeds of dilation.

The dotted line is the differential curve of the dilation to a sound stimulus of the normal pupil (evenly ascending and descending curve); the solid line, the differential curve of the dilation to a sound stimulus of the sympathectomized and hypersensitive pupil (straight line).

again, and in about three seconds it reached the diameter it had had before the sound stimulus became effective. In contrast thereto, the sympathectomized and hypersensitive pupil continued to dilate at an even rate for 2.5 seconds (1.5 mm., i. e., 0.6 mm. per second). Since the nonsympathectomized pupil, during this 2.5 seconds, was already recontracting, the sympathectomized pupil became larger than the nonsympathectomized one (fig. 10 *A*, *b* to *c*).

It is evident, therefore, that reflex dilation, in the stricter sense, and delayed dilation, i. e., the dilation caused by the effect of epinephrine on the denervated dilator muscle, are two different movements; they go on at different rates of speed, and not simultaneously. The direct reflex dilation, due to relaxation of the third nerve, is slow and inextensive; the simultaneous reflex dilation, due to sympathetic reflex activity, is fast and extensive (fig. 10 *A*, *a* to *b*). The delayed dilation, present exclusively on the sympathectomized side and due to hypersensitivity to epinephrine of the denervated dilator muscle, is slow (fig. 10 *A*, *b* to *c*).

When the animal is in a condition of emotional indifference and hypersensitivity of the sympathectomized iris is present, the sympathectomized pupil is smaller than the nonsympathectomized one. When the animal becomes suddenly excited, an immediate and fast dilation movement sets in on the normal side. It is always at least four times as extensive, and has ten to twelve times as high a rate of speed, as the corresponding dilation of the sympathectomized side. However, a slow, long-lasting secondary dilation sets in in the hypersensitive sympathectomized pupil, with the result that it becomes, for some time, larger than the normal pupil.

Characteristic differences exist between the dilation movements of the normal and those of the hypersensitive denervated iris. These differences are best shown by the differential analysis of the movements (fig. 10 *B*). The differential curve (curve of speeds) of dilation of the normal pupil shows fast acceleration, followed by deceleration, of the speed of dilation; in contrast to this, the hypersensitive sympathectomized pupil dilates at an even speed. Its differential curve, therefore, is represented by an almost straight line. This means that the mechanism by which in denervated hypersensitive tissues sensory stimuli become effective is different from that of nervous control.

6. *Removal of Ciliary Ganglion and Sympathetic Reflex Activity.*—Ury and Gellhorn,[6] Seybold and Moore [8] and Kuntz and Richins [13] stated that the parasympathectomized pupil was large but not at its maximal dilation. Our experiments on cats in which the ciliary ganglion had been removed unilaterally from forty-eight hours to three weeks prior to the experiments confirmed these findings. We wish to add that when the animal was observed under the condition of light a strong anisocoria existed. This anisocoria was maximal under intense illumination and decreased in proportion to the decrease in intensity of the light; in total darkness the anisocoria disappeared almost completely, the difference becoming as little as 0.1 to 0.2 mm. This means that in total darkness the normal pupil behaved similarly to the para-

sympathectomized one and that the parasympathetic tonus, which decreases with decreasing intensity of light, is practically absent in darkness.

However, in contrast to the statements of these authors, psychosensory stimulation by means of weak stimuli, such as sound, blowing into the face or pinprick, resulted in pupillary dilation, which could in each case be recorded pupillographically.

Figure 11 *A* illustrates these observations. The cat was resting comfortably and without recognizable emotions. After adaptation to total darkness for about three minutes, the camera and illumination with red–infra-red light were started simultaneously. Before the light caused the normal pupil to contract, the diameters of both pupils were

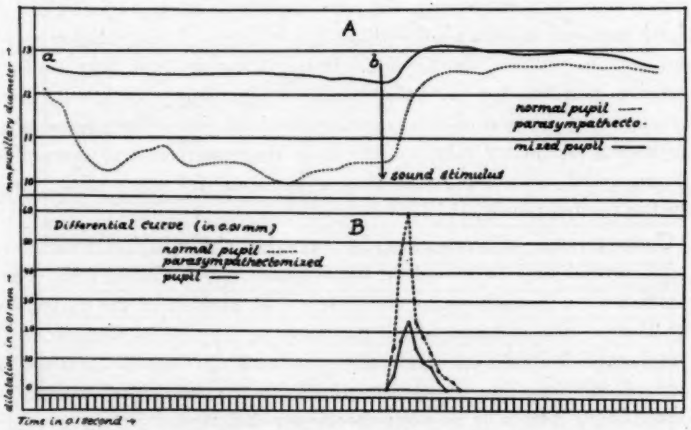

Fig. 11.—Reaction to a sound stimulus in a cat in which, three weeks previously, the right ciliary ganglion had been removed.

A, pupillary reaction to infra-red–red light (*a*-*b*) and to a sound stimulus (at *b*). The upper (solid) line is the pupillogram of the parasympathectomized pupil; the lower (dotted) line, the pupillogram of the normal pupil. The parasympathectomized pupil did not contract to the light stimulus but dilated in response to the sound stimulus. The normal pupil contracted to the light stimulus and dilated to sound stimulus.

B, differential curve showing increase and decline of speeds of dilation. The dotted line is the differential curve of the dilation of the normal pupil, and the solid line, the differential curve of the dilation of the parasympathectomized pupil, to a sound stimulus. The two curves, although different in dimension, are equal in shape.

very large (normal pupil, 12.1 mm.; parasympathectomized pupil, 12.8 mm.). The light stimulus caused contraction of the normal pupil to about 10.3 mm. When, at *b*, the sound stimulus was given, it resulted in bilateral reflex dilation, which, though reduced in extent in the parasympathectomized, large pupil, showed the same shape of movement on the two sides; this phenomenon can be seen directly from the pupil-

lographic curve, but is even more evident in the differential curve, which shows identical periods of acceleration and deceleration in the two curves. This means that the same process, with the same type of nervous control, is at work on the two sides. Since on one side the parasympathetic nerve supply was absent, both movements must be due to sympathetic reflex activity only.

We recorded, in parasympathectomized pupils, spontaneous fluctuations (up to 1 mm.) of the pupillary diameter which were roughly parallel with, although less extensive than, those of the normal pupil (fig. 12). Since the parasympathetic nerve supply was removed, these movements must be due to sympathetic activity running over the peripheral sympathetic nerve fibers; it is quite possible, although not proved in our experiments, that they are due to spontaneous fluctuations

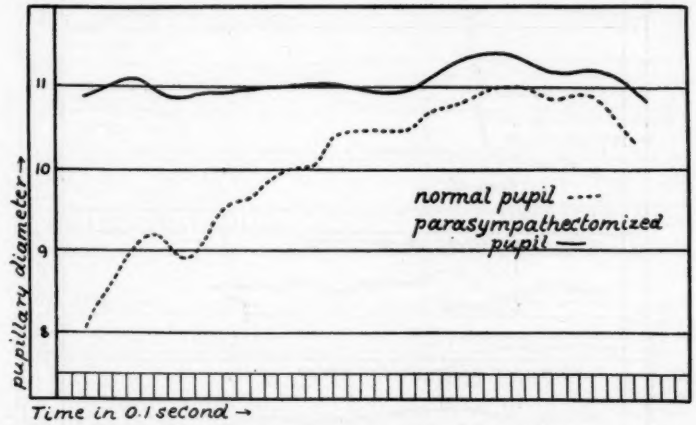

Fig. 12.—Spontaneous pupillary movements in a cat in which, three days previously, the right ciliary ganglion had been removed.

The upper (solid) line is the pupillogram of the parasympathectomized pupil; the lower (dotted) line the pupillogram of the normal pupil.

The parasympathectomized pupil showed spontaneous movements, which were due exclusively to sympathetic activity. Analogous movements could be seen in the normal pupil (dotted line).

Comparison of the two curves shows which movements are due to sympathetic and which to parasympathetic activity.

in the emotional state of the animal. The statements by Seybold and Moore [19] that "under ordinary conditions sympathetic dilator tone is remarkably constant while third-nerve constriction is subject to extreme reflex modification" and, further, that "consequently changes in the size of the pupil depend upon reflex variations in the activity of the oculomotor nerve" are incompatible with our recordings of pupillary movements in parasympathectomized cats.

18. Footnote deleted.

19. Seybold and Moore,[8] p. 440.

7. Influence of Physostigmine on Sympathetic Reflex Activity.—As mentioned before, Ury and Gellhorn used physostigmine for constriction of the mydriatic pupil in cases in which the third nerve was sectioned but the sympathetic nerve supply was unimpaired. They did so in order to cause the pupil to contract, thus giving it a better chance to dilate in response to psychosensory stimuli. They found that the parasympathectomized, physostigminized and thereby contracted pupil did not dilate to psychosensory stimulation, although the sympathetic nerve was not impaired and the threshold of pupillodilator fibers to electrical

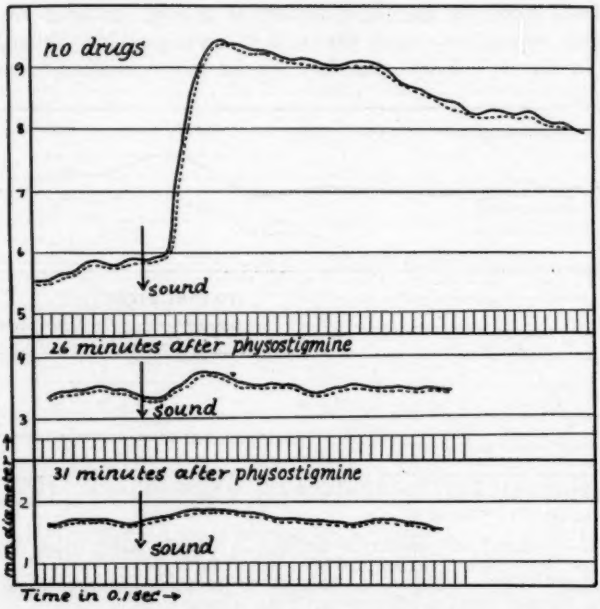

Fig. 13.—Pupillary reflex dilation in a normal cat before and after instillation of 2 drops of a 1 per cent solution of physostigmine salicylate into each conjunctival sac.

Upper curve, normal reaction (extensive dilation) of both pupils to a sound stimulus.

Middle curve, twenty-six minutes after instillation of physostigmine. Both pupils dilated in response to a sound stimulus only about one-eighth the original reaction.

Lower curve, five minutes later, i. e., thirty-one minutes after instillation of physostigmine. The dilation to a sound stimulus has almost disappeared.

stimulation was extremely low and was not altered by physostigmine. Seybold and Moore found that "during the stages of partial eserinization the pupil of the normal eye dilated instantly in response to the stimuli listed [dark adaptation, painful stimulation and emotional excitement], but . . . after the eserine effect was complete the dilator response of

the normally innervated iris was usually reduced and in some instances abolished." [20] Therefore, and because Ury and Gellhorn's statement was in disagreement with numerous clinical experiences in man, we raised the question of whether or not the pupil really had maintained the same threshold values for physiologic sympathetic stimuli after physostigminization.

In normal cats, we instilled 2 drops of a 1 per cent solution of physostigmine salicylate into the conjunctival sac of each eye. While the contraction to physostigmine developed, we recorded at intervals the pupillary responses to sensory stimuli (sound). We found (fig. 13 *A*) in the typical case of a normal cat a dilation to a sound stimulus

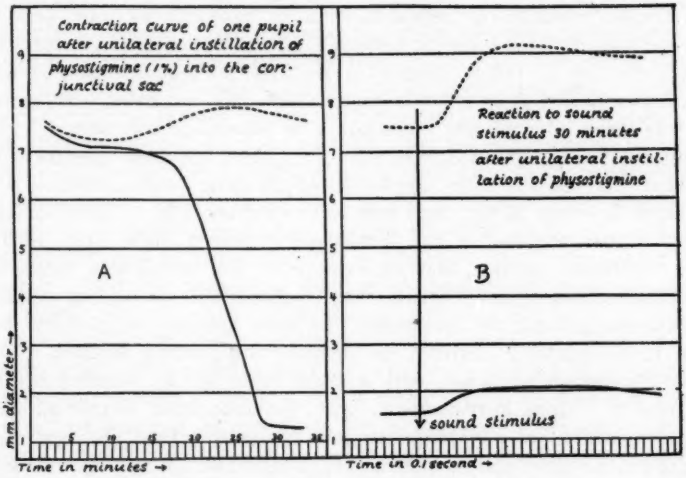

Fig. 14.—Effect of unilateral instillation of 3 drops of a 0.25 per cent solution of physostigmine salicylate into the conjunctival sac of a normal cat.

A, physostigmine contraction curve during thirty-five minutes subsequent to instillation of physostigmine into the conjunctival sac of one eye. The real contraction (at an average speed of about 0.4 mm. per minute) started about fourteen minutes after instillation of the first drop of physostigmine and was completed fourteen minutes later. The ordinate represents pupillary diameter, in millimeters; the abscissa represents time, in minutes.

B, pupillary reflex dilation, of about 0.5 mm., in response to a sound stimulus thirty minutes after instillation of physostigmine, as compared with dilation of about 1.7 mm. of the nonphysostigminized pupil. The ordinate represents pupillary diameter, expressed in millimeters; the abscissa, time, expressed in intervals of 0.1 second.

of 3.6 mm.; twenty-six minutes after instillation of the drug the pupils had contracted from 6 to 3.3 mm. The reflex dilation to sound was reduced to 1.5 mm. Five minutes later, i. e., thirty-one minutes after

20. Seybold and Moore,[8] p. 439.

the instillation of physostigmine, the pupil had reached full contraction (1.6 mm.), and the dilation to sound stimuli had faded to 0.28 mm., i. e., to practically zero.

In a second series of experiments, we instilled physostigmine into the conjunctival sac of the right eye only. While unilateral contraction to physostigmine developed, we recorded the responses to mild (motor noise) and loud (pistol shot) acoustic stimuli. With mild sensory stimuli which produced a dilation of about 1 mm. in the nonphysostigminized pupil, a reduction in response on the physostigminized side appeared nineteen minutes after instillation, at the moment when the contraction to physostigmine began (fig. 14 *A*). This reduction of reflex dilation to mild sensory stimuli increased progressively.

While reduction of reflex dilation in response to mild sensory stimuli started about nineteen minutes after instillation of physostigmine, the reduction of reflex dilation in response to loud acoustic stimuli became apparent only a few minutes later. No reduction was shown twenty-three minutes after instillation of physostigmine, although the right pupil had contracted from 8.2 to 5.1 mm.; but three minutes later (twenty-six minutes after instillation of the drug) reflex dilation was reduced to about 50 per cent, and seven minutes later to about 25 per cent, of the reaction of the nonphysostigminized pupil (fig. 14 *B*). We therefore conclude that excitability of the sympathetic nerve to electrical stimuli is not identical with its excitability to natural stimuli.

Physostigminization diminished not only sympathetic activity, but also parasympathetic activity, for instance the reaction to light. The nonphysostigminized pupil, with a diameter of 8 mm., showed a contraction to 5.3 mm. in response to light; the same pupil, sixteen minutes after instillation of physostigmine into the conjunctival sac, had contracted to 5.8 mm., and its contraction to light had not only become less extensive (3.3 mm.) but also had changed its shape, having become more sluggish. This shows that the reflex activity of both the sympathetic and the parasympathetic system is diminished when the pupils are under the influence of physostigmine.

COMMENT

Section of the cervical sympathetic nerve fibers, either preganglionic or postganglionic, is followed by immediate homolateral dilation of the pupil, due to stimulation resulting from the severing of the nerve. Any further pupillary movements, contractions or dilations occurring after the sympathetic nerve has been cut can no longer be due to impulses running over it. The slow contraction movement which follows the immediate dilation lasts over a period of one to three minutes. It is not a movement of even speed; the evenness of speed is interrupted by periods in which the contraction movement becomes slower or comes

to a standstill or, at more or less regular intervals, turns into its opposite, namely, dilation. Therefore the contraction movement occurs in waves. The interruptions in the even movement of contraction can no longer be due to impulses running over the cervical sympathetic fibers but must be due to parasympathetic constricting or relaxing influences. They are directed toward the substitution of the former parasympathetic-sympathetic equilibrium by a pupillary condition which is exclusively controlled by the parasympathetic nerve system.

The dilation and subsequent contraction which the pupil performs immediately after sympathectomy do not influence the contralateral, normal pupil. All contraction or dilation movements which, after unilateral sympathectomy, concern the two eyes equally are due to innervating, relaxing or inhibitory influences of the central parasympathetic system. Such movements can be observed particularly at moments when the ether anesthesia becomes light and the animal starts to awake. Sympathectomy disinhibits, and thereby facilitates, all parasympathetic activity; this explains the seemingly paradoxic phenomenon that spontaneous contractions and dilations occur which are slightly more extensive in the sympathectomized pupil than in the normal one.

Immediately before death the pupils contract. After about 20 seconds of contraction a dilation occurs, which in unilaterally sympathectomized cats is almost equal on the two sides; after about 50 seconds of dilation, when the dilation of the sympathectomized pupil has almost come to an end, the nonsympathectomized pupil performs another strong dilation, resulting in nearly maximal dilation of the healthy pupil. This additional dilation (of nearly 2 mm.) of the normal pupil at the moment of death is due to reflex activity of the sympathetic nerves and therefore is absent on the sympathectomized side. In the case of hypersensitivity to epinephrine after postganglionic sympathectomy, the sensitized pupil exceeds the normal one in its final dilation preceding death. This indicates output of epinephrine at the moment of death.

The reflex to light is definitely influenced by sympathectomy, which tends to increase the contraction and reduces the secondary redilation phase after contraction to light.

Psychosensory stimuli cause the cat's pupil to dilate. This dilation varies in extent from animal to animal. It also varies in the same animal, depending on the intensity of the stimulus, the emotional condition of the cat at the moment of the stimulus and the intensity of illumination present at the time of stimulus. It diminishes progressively when, under illumination of low intensity, the pupils become very large. It approaches a minimum while the diameter of the pupil approaches a maximum; this is true not only of pathologically mydriatic, such as parasympathectomized pupils, but also of normal pupils physiologically dilated by the condition of darkness.

The active sympathetic reflex dilation of the pupil accounts for from four fifths up to nine tenths of the total extent of dilation, while less than one fifth of the total amount of dilation is due to influences of the third nerve. The dilation in the case of hypersensitivity of a denervated pupil is quite different from the dilation due to sympathetic reflex activity. The latter produces shapes of dilation showing a characteristic increase and decline of speed; its curves are similar to those produced by direct stimulation of the peripheral sympathetic fibers, for instance, by sectioning; the former goes on at an even speed, the differential curve of which is represented by a straight line. It seems as though two different mechanisms were at work—one of peripheral action under nervous control, another of peripheral action without direct nervous control.

Active sympathetic reflex dilation could be recorded after the ciliary ganglion had been removed. Although it was reduced in extent—a phenomenon which may be explained by the size of the mydriatic pupil—its differential curve showed the same shape as did the curve for the dilation of the normal pupil. Thus, we found that active sympathetic reflex dilation really exists; compared with it, the dilation due to relaxation of the third nerve is a practically negligible quantity.

In normal pupils, physostigmine reduces the extent and diminishes the speed of all reflexes, both sympathetic and parasympathetic. Reflexes to weak physiologic stimuli are more readily suppressed than reflexes to strong stimuli. We conclude, therefore, that physostigminization normally creates conditions unfavorable to the study of sympathetic action. This may account for the failure of other authors to produce sympathetic reflex dilation by means of physiologic stimuli in parasympathectomized and physostigminized pupils, whereas powerful stimuli, such as a metrazol® convulsion or electrical stimulation of the sympathetic nerve trunk, still produced pupillary dilation.

It is true that in parasympathectomized pupils, as well as in normal pupils mydriatic after adaptation to darkness, the active sympathetic reflex dilation, although normal in shape, may be greatly reduced in extent. The most apparent explanation would be the possible mechanical limitation of the mydriatic pupil for further dilation. However, we cannot accept this as the sole explanation; dynamic factors may also play a role. In order to explain this statement, we wish to mention a number of clinical observations which may throw light on the problem. First, we observed a case of syringomyelia with unilateral periodic sympathetic spasm and relaxation.[21] Periodic dilation and recontraction of the left pupil and palpebral fissure occurred about once every five minutes.

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21. Lowenstein, O., and Levine, A. S.: Pupillographic Studies: V. Periodic Sympathetic Spasm and Relaxation and Role of Sympathetic Nervous System in Pupillary Innervation, Arch. Ophth. **31**:74-94 (Jan.) 1944.

By means of a timing system it was possible to elicit all types of pupillary reflexes, particularly light reflexes and reflexes to psychosensory stimuli, at any phase of the active dilation and the reactive contraction period. It was found that a certain functional sympathetic tonus was necessary to elicit an optimal sympathetic reaction, for example, a psychodilation reflex; on the other hand, a certain well defined degree of sympathetic innervation or tonus was also necessary to elicit an optimal parasympathetic reaction, such as a light reflex. These facts suggest the possibility that a certain well defined parasympathetic tonus might be necessary to make an optimal sympathetic reaction possible and that the lack of parasympathetic tonus represents an unfavorable condition for the eliciting of a sympathetic reflex.

This conclusion was supported by findings in another clinical case,[22] one of cyclic oculomotor paresis. Such cases are well known. As far back as 1939, Bielschowsky [23] stated that 32 cases of this type were found in the literature. In our case the left pupil contracted periodically while the homolateral eyelid retracted; after the contraction had come to an end, the pupil dilated and homolateral ptosis developed. When the pupil came into its spastic phase, it required five seconds to reach its greatest contraction; when the spasm of the sphincter iridis relaxed, the pupil took nine seconds to reach full dilation. By applying the same timing system as in the case aforementioned, we examined this patient in the various stages of constriction and relaxation. It was found that while the pupil was moving from contraction to relaxation, the light reflex, which was absent at full contraction, started to appear when the pupil reached a diameter of about 4 mm. and reached a maximum at about 7 mm., to decrease again when the pupil dilated further. On the other hand, the dilation reflex to a sound stimulus was absent when the pupil was very small, increased while the pupil dilated, reached its maximum when the pupillary diameter was about 6 mm. and decreased again while the pupil dilated further. This observation proves that the sympathetic reflex dilation, and parasympathetic reflexes as well, at least in man, depend on the tonus of the constrictor muscles of the pupil. Loss of tonus, as well as increased tonus above a certain degree, are unfavorable; absence of tonus, as well as maximal tonus, does not allow the reflex to appear.

This observation gives the key to the explanation of the fact that psychosensory dilation reflexes are reduced in extent in parasympa-

22. Lowenstein, O., and Givner, I.: Cyclic Oculomotor Paralysis (Spasmus Mobilis Oculomotorius), Arch. Ophth. **28**:821-833 (Nov.) 1942.

23. Bielschowsky, A.: Ueber die Oculomotoriuslähmungen mit cyclischem Wechsel von Krampf- und Erschlaffungszuständen am gelähmten Auge, Arch. f. Ophth. **121**:659-685, 1929; Lectures on Motor Anomalies: IX. Oculomotor-Nerve Paralyses and Ophthalmoplegias, Am. J. Ophth. **22**:484-498 (May) 1939.

thectomized pupils. It proves the great importance of the level of sympathetic-parasympathetic equilibrium and the mutual dependence of sympathetic and parasympathetic reflexes. It may be mentioned that strong sympathetic innervation is able to suppress the parasympathetic reflex in cats as well as in man. Clinically, the so-called *Angst* (anxiety) pupil described by Bumke, which does not react to light, is known to occur in normal persons, and Westphal's [24] *Spasmus mobilus* is observed in patients with catatonia, who, under the influence of emotions, show complete pupillary immobility to light at one time and good reactability a few seconds later, when the emotion has subsided.[25]

The statement of Ury and Oldberg [7] that "none of the variability of the pupil to light or afferent stimuli is lost when the sympathetic component is interrupted, but the magnitude of the reaction is diminished" is not corroborated by our findings. We observed that the magnitude of the response to light in the cat's sympathectomized pupil is increased regularly at the first reaction, frequently at the second reaction and often at following reactions. It is true that under the influence of repetition this magnifying effect is lost, or even reversed, but the discussion of this effect is not within the scope of this paper.

The pupillographically recorded fact that the parasympathectomized pupil is still subject to spontaneous contractions and dilations shows that the role of the sympathetic nerve fibers in relation to the dilator muscle does not differ from that of the parasympathetic fibers in relation to the constrictor muscle of the pupil, except for the specific differences of sympathetic and parasympathetic innervation and quantitative differences.

SUMMARY AND CONCLUSIONS

Section of the cervical sympathetic trunk results in immediate dilation of the homolateral pupil, followed by contraction leading to permanent anisocoria. The homolateral dilation is due to stimulation of the severed fibers by the act of cutting. The shape of the movement and the curve of its speed (differential curve) are identical in all details with the corresponding aspects of the dilation movement obtained by sensory or purely emotional stimulation of the normal animal when awake. The total dilation lasts 0.5 to 0.6 second; it is followed by a slow contraction movement of uneven speed. The continuity of this movement is inter-

24. Westphal, A.: Ueber Pupillenphänomene bei Katatonie, Hysterie und myoklonischen Symptomenkomplexen, Monatssch. f. Neurol. u. Psych. **47**:187-193, 1920.

25. Löwenstein, O.: Experimentelle Beiträge zur Lehre von den katatonischen Pupillenveränderungen, Monatssch. f. Psychiat. u. Neurol. **47**:194-215, 1920. Löwenstein, O., and Westphal, A.: Experimentelle und klinische Studien zur Physiologie und Pathologie der Pupillenbewegungen, mit besonderer Berücksichtigung der Schizophrenie, Berlin, S. Karger, 1933.

rupted by periods of slower contraction, of standstill or even of redilation. The whole movement lasts from 50 to 300 seconds and is due exclusively to impulses running over the third nerve. Its wave-shaped course gives a picture of the adaptation process by which the sympathetic-parasympathetic equilibrium, in existence before section of the cervical sympathetic trunk, is replaced by a new condition exclusively controlled by parasympathetic innervation, relaxation or inhibition.

The purely parasympathetic control of sympathectomized pupils is modified by influences which develop when denervation is followed by sensitization. The mechanism of pupillary dilation due to these influences differs from that due to active sympathetic innervation, as shown by differences in shape and speed (differential curve) of the movements.

Active reflex dilation of the pupil is present at the moment of death on the normal side and absent on the sympathectomized side; in case of hypersensitivity to epinephrine after postganglionic sympathectomy, the sympathectomized pupil dilates and finally reaches a larger diameter than that of the normal pupil.

After sympathectomy, movements due to stimulation and relaxation of the third nerve may be stronger on the sympathectomized side than on the normal side. This is explained as a disinhibition phenomenon of the third nerve, due to the absence of the cervical sympathetic nerve supply.

This disinhibition modifies the contraction to light, which generally is more extensive on the sympathectomized side than on the normal side. This phenomenon tends to disappear on repeated stimulation with light.

The secondary redilation after contraction to light is predominantly due to sympathetic influences passing over the cervical sympathetic fibers.

Approximately four fifths of active reflex dilation is abolished when the cervical sympathetic trunk is cut; this means that, normally, four fifths of active reflex dilation runs over the peripheral sympathetic nerve fibers and only about one fifth is produced by central inhibition of activity of the third nerve. The extent of active reflex dilation depends on the intensity of the stimulus, the emotional condition of the animal and the level of illumination; in cases in which these factors are equal, the initial diameter, as the expression of the sympathetic-parasympathetic equilibrium present at the moment of the psychosensory stimulation, determines the extent of reaction.

When hypersensitivity has developed in the denervated iris, the psychosensory dilation consists of two phases: (*a*) slow and inextensive dilation, which seems analogous to the psychosensory dilation found in cases of sympathectomy without hypersensitivity, and described as due to inhibition of the third nerve nucleus, and (*b*) a slow, long-lasting and therefore extensive dilation, beginning about 0.6 second after the

stimulus. This dilation may continue while the normal pupil is already recontracting. It causes the sympathectomized pupil to become larger than the normal one, thereby producing the classic picture known as paradoxic pupillary dilation.

The mechanism by which in the denervated iris tissue sensory stimuli lead to dilation of the pupil is different from the mechanism of normal pupillary dilation under nervous control. This difference is shown in the differential curve, which, for the normal pupillary dilation is represented by an ascending and a descending line, and in the case of hypersensitivity in which direct nervous control is absent, by a straight line on the abscissa.

In cats in which the ciliary ganglion has been removed, weak psychosensory stimuli result in pupillary reflex dilation, both of the normal and of the parasympathectomized pupil. These dilation movements, although less extensive on the parasympathectomized than on the normal side, are identical in shape and dynamic structure on the two sides. Therefore they are considered to be due to the same reflex mechanism, which is sympathetic in nature.

In parasympathectomized cat pupils, bilateral and roughly parallel spontaneous movements are observed. They are due to variations in the sympathetic dilator tone, possibly accompanying emotions. They are usually more extensive on the normal side, at least when recorded under the condition of light.

Parasympathetic constrictor tone increases with increasing intensity of light and decreases with diminishing intensity of illumination. A nearly complete parasympathetic relaxation seems to occur in complete darkness, the diameter of the dark-adapted normal pupil thus approaching that of the parasympathectomized pupil.

Physostigminization not only contracts the pupil but reduces and modifies all pupillary reactions, both sympathetic and parasympathetic. In physostigminized pupils weak physiologic stimuli lose their effect more readily than powerful stimuli.

In the variability of sympathetic and parasympathetic tonus, a certain sympathetic-parasympathetic relation exists which is most favorable, and another which is least favorable, for the production of sympathetic and/or parasympathetic reflexes. Complete, or almost complete, absence of tonus, such as existed in cases of severed parasympathetic fibers, appears to be unfavorable to the production of active sympathetic reflexes. Physostigmine or other parasympathomimetic drugs, and parasympatholytic and sympatholytic drugs as well, generally do not favor the development of a natural and optimal sympathetic-parasympathetic relation.

MUTUAL ROLE OF SYMPATHETIC AND PARASYMPATHETIC IN SHAPING OF THE PUPILLARY REFLEX TO LIGHT

Pupillographic Studies

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IN NUMEROUS pupillographic experiments made for clinical purposes we found various shapes of the pupillary reflex to light in conditions which, from clinical evidence, were due to pathologic processes or lesions of different localizations. The shapes varied, whether the lesions were in the autonomous centers or the periphery, either sympathetic or parasympathetic. Therefore it is the purpose of these studies to determine, by means of experimental lesions at the various levels of the reflex arc in some mammals, the sympathetic and/or the parasympathetic factors which are furnished, at these levels, to the integration of the normal shape of the pupillary reflex to light, with the goal of providing a comparative localization basis for pupillography as a tool of differential diagnosis of clinical lesions of the autonomic nervous system.

METHOD

We used 24 cats, 12 monkeys (Macaca mulatta) and 25 rabbits. Of the cats, 7 were not operated on; 7 were examined both while normal and after unilateral preganglionic sympathectomy, and 6 were examined both while normal and after unilateral postganglionic sympathectomy. Three were examined both while normal and after preganglionic sympathectomy on one side and postganglionic sympathectomy on the other side; in these 3 cats the two operations were performed at the same time. One cat was examined after partial crushing of the ciliary ganglion. Of the monkeys, 1 was not operated on; 3 were examined after unilateral removal of the superior cervical ganglion, and 2 of these 3 monkeys were again examined after an ipsilateral lesion in the hypothalamus was added to the peripheral sympathetic lesion. Four monkeys were examined both while normal and after bilateral hypothalamic lesions. In 1 monkey, a lesion was placed in the third nerve nucleus, and in 3 monkeys the ciliary ganglion was slightly crushed and allowed to regenerate. The central lesions were made by means of the Horsley-Clarke equipment; stimulation of the hypothalamus produced bilateral

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dilation of the pupils, but no attempt was made to record pupillographically the pupillary movements immediately following stimulation.

In addition to 22 normal rabbits, 3 rabbits were examined both while normal and after alcohol was injected intraorbitally into the region of the ciliary ganglion. The pupillary reaction to light, which was completely absent in 1 rabbit and almost absent in 2 rabbits two days after the operation, was followed up while the third nerve recovered.

Pupillographic experiments were made after the animals had fully recovered from the operation. These studies consisted of recording of pupillary reflexes to light. Procedure and equipment were described in a former publication.[1]

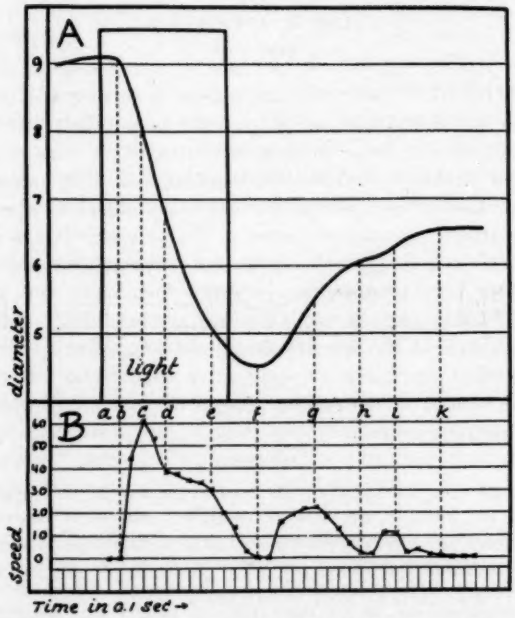

Chart 1.—Reaction to light in a normal nonexcited cat. Pupillogram (*A*) and differential curve (*B*).

(*A*) The pupillary diameter (in millimeters) is plotted against time (in 0.1 second). After a latency period of about 0.2 second, the pupil contracts vigorously (4.7 mm. in 1.4 second). Redilation, which occurs in two phases, is relatively slow and inextensive, recovering only 2 mm. of the pupillary diameter (redilation block).

(*B*) Contraction and redilation within each successive tenth of a second are plotted (in 0.01 mm.) against time (in 0.1 second).

(*a-b*) Latency period for contraction; (*b-c*) ascending branch of C wave (period of increasing contraction speed); (*c-f*) descending branch of C wave (period of decreasing contraction speed); (*f-g*) ascending and (*g-h*) descending, branches of D wave (increase and decrease of speed of primary dilation phase); (*h-i*) ascending, and (*i-k*) descending, branches of E wave (increase and decrease of speed of secondary redilation phase).

1. Lowenstein, O., and Loewenfeld, I. E.: Role of Sympathetic and Parasympathetic Systems in Reflex Dilatation of the Pupil: Pupillographic Studies, Arch. Neurol. & Psychiat. this issue, p. 313.

About 400 series of light reactions were recorded, but in this paper our attention will be directed mainly to the first reaction to light in each series. Pictures were taken, as mentioned before, at a rate of 10 per second, under dark red–infra-red illumination, to which the animals were adapted before light stimuli were applied. The light stimulus lasted one second, and the dark interval between light stimuli, three seconds; this means that 40 pictures were measured on each side for each reaction.

As in the cases of reflex dilation,[1] the pupillograms of the reflexes to light were further studied by differential analysis (differential pupillography). The extent of contraction or redilation within each successive tenth of a second was plotted as the ordinate (in 0.01 mm.) against time as the abscissa (in 0.1 second). The resulting differential curve shows the increase and decrease of speed of motions. These differential curves were studied in relation to the original pupillographic curves.

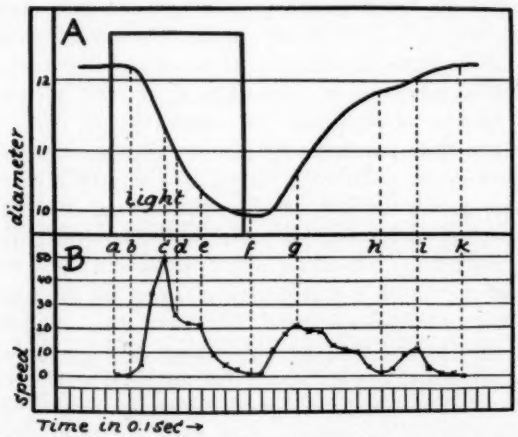

Chart 2.—Pupillogram (*A*) and differential curve (*B*) of the reaction to light in the same cat as that whose reactions are shown in chart 1, but taken during excitement.

(*A*) The pupillary diameter has increased to 12.2 mm. Contraction is decreased; redilation is undisturbed.

(*B*) The entire C wave is reduced; its peak is delayed. D and E waves are fully developed.

RESULTS

1. *Reflex to Light in Normal Cats.*—In normal cats the direct and the indirect (consensual) reactions to light are generally found to be almost or fully identical. Two different types of the light reflex are found, the details of which depend on the emotional state of the animal at the moment of the light stimulus.

When the animal is calm (chart 1), the diameter of the dark-adapted normal pupil amounts to between 8 and 12 mm. After a latency period of about 0.2 second, an enormous contraction takes place, measuring from about 4 to 7 mm. It lasts about 1.2 to 1.6 seconds.

When the contraction has come to an end, redilation starts. This redilation lasts more than 2 seconds; it is therefore much slower than the preceding contraction. Redilation extends to about half or less of the preceding contraction. This means that in normal nonexcited cats, redilation is blocked and the pupil does not recover its original diameter but levels off about midway.

However, when the animal is excited (charts 2 and 3), the diameter of the pupil may increase to 14 mm., or even more. The contraction to light is less extensive than in nonexcited cats. The degree to which the contraction is diminished varies from only slight reduction to one half, one third or, in extreme cases, one tenth or even less, of the contraction in nonexcited animals. The redilation is not blocked at all. Its extent may be the same as, or even greater than, the preceding contraction.

Instead of the block in redilation of the nonexcited animal, we find in excited cats an inhibition of contraction, which may, in cases of strong excitement, lead to complete block of contraction.

When we analyze pupillograms, such as that shown in charts 1, 2 and 3, by drawing the differential curves, we find certain characteristics. We shall first consider the case of a nonexcited normal cat (chart 1 *A* and *B*). The speed of contraction reaches a peak 0.4 second after the light stimulus has started (*a*), and then gradually decreases (*c-f*). The decrease is represented not by an evenly declining curve, but by a curve which generally shows at least one, and sometimes two, inhibition points (*d* and *e*); this means that the deceleration of pupillary contraction speed is not performed gradually, but that the pupil, at times, maintains a uniform contraction speed for several tenths of a second. The redilation is characterized by an increase (*f-g*) and a decrease (*g-h*) of speed. This is followed by a second—generally shorter and less extensive—period of increased (*h-i*) and decreased (*i-k*), speed of redilation. We call the portion from *b* to *f* the C wave (contraction wave), that from *f* to *h* the D wave (primary redilation wave) and from *h* to *k* the E wave (secondary redilation wave). The ascending branch of the C wave (*b-c*) corresponds to the "primary" contraction phase; the descending branch (*c-f*), to the "secondary" (and "tertiary") contraction phase, of earlier publications.[2]

2. (*a*) Lowenstein, O., and Levine, A. S.: Pupillographic Studies: V. Periodic Sympathetic Spasm and Relaxation and Role of Sympathetic Nervous System in Pupillary Innervation, Arch. Ophth. **31**:74-94 (Jan.) 1944. (*b*) Lowenstein, O., and Schoenberg, M. J.: VI. Pupillary Reactions of the Seemingly Unaffected Eye in Clinically Unilateral Glaucoma: Pupillary Contributions to Diagnosis of Glaucoma in the Preclinical Stage, ibid. **31**:392-398 (May) 1944; (*c*) VII. Nervous Factor in the Origin of Simple Glaucoma, ibid. **31**:384-391 (May) 1944.

When the same normal cat is excited, the differential curve (chart 2 *B*) shows the peak of contraction speed (*c*) both reduced (0.50 mm., instead of 0.62 mm.) and delayed (0.5 second, instead of 0.4 second) after the start of the light stimulus. The descending part of the C wave shows the same inhibition as in the case of chart 1. The redilation waves (D and E waves) are larger in proportion to the C wave than those for the same animal when not excited.

In case of strong excitement (chart 3 *A* and *B*), when the whole reaction to light—both contraction and redilation—becomes very sluggish and inextensive, the C wave, as well as the D and E waves, are reduced to a fraction of their former extent, and the relation $\frac{C}{D+E}$ is shifted in favor of the redilation waves.

2. *Influence of Peripheral Sympathectomy on the Reflex to Light and the Development of Anisocoria in Cats.*—In analogy with our

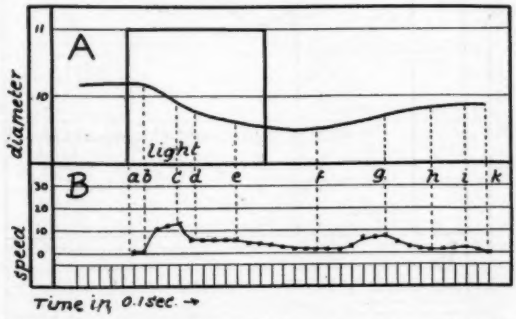

Chart 3.—Pupillogram and differential curve of the reaction to light in a highly excited cat.

(*A*) The entire reaction to light is sluggish and inextensive.

(*B*) All waves are reduced; the C wave is delayed. The normal proportion $\frac{C}{D+E}$ of waves (chart 1) is shifted in favor of the redilation waves.

terminology as used clinically, we call anisocoria which is always present, both when the pupil is at rest and when it is in motion, "static anisocoria"; anisocoria which develops or increases during contraction to light is called "dynamic contraction anisocoria"; anisocoria which develops or increases during active sympathetic reflex dilation is called "dynamic dilation anisocoria," and anisocoria which develops during redilation after contraction to light is called "dynamic redilation anisocoria."

In cats with preganglionic sympathectomy and in cats with postganglionic sympathectomy in which hypersensitivity to epinephrine has not yet developed in the denervated iris, we find static anisocoria. The sympathectomized pupil is the smaller one. The anisocoria may

amount to from less than 2 to more than 6 mm. and is more pronounced when the cat is excited than when it is calm. In cats with postganglionic sympathectomy and hypersensitivity to epinephrine, the sympathectomized pupil is also smaller than the normal one as long as the animal is calm. However, under the influence of excitement anisocoria decreases and may even reverse, the sympathectomized and hypersensitive pupil becoming larger than the normal one.

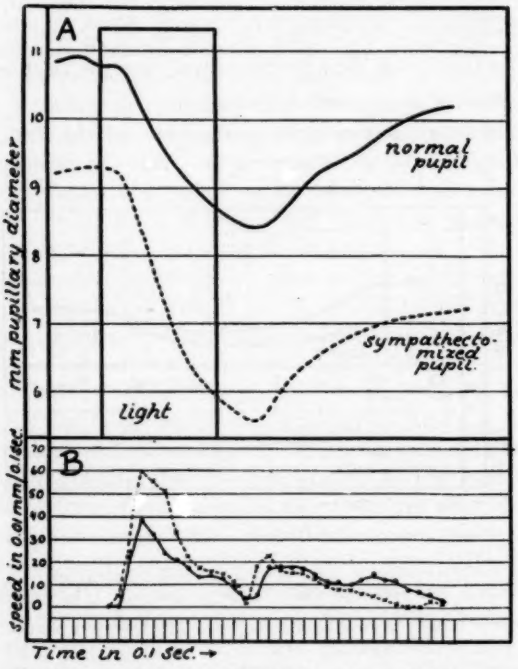

Chart 4.—Pupillogram (*A*) and differential curve (*B*) of the reaction to light in a cat with unilateral postganglionic sympathectomy, taken when calm.

(*A*) Anisocoria, of 2 mm., with the sympathectomized pupil the smaller one, increases during contraction; contraction is more extensive and faster in the sympathectomized pupil.

(*B*) C and D waves are increased and shifted to the left, and the E wave is greatly reduced on the sympathectomized side (broken line).

In cats with preganglionic sympathectomy, in cats with postganglionic sympathectomy without hypersensitivity and in cats with postganglionic hypersensitivity which are calm, the reaction to light shows the following characteristics:

The latency period for contraction to light is slightly shorter than that of the normal pupil. The contraction speed is, from the beginning,

higher than that on the normal side. Full contraction, which is frequently somewhat more extensive on the sympathectomized side, is reached (between 0.1 and 0.3 second) earlier than on the normal side. Anisocoria may increase during the contraction to light, since the contraction of the sympathectomized pupil is disinhibited.

Sympathectomy, in general, favors the development of a redilation block, since the secondary redilation phase is greatly reduced as compared with the normal pupil.

The differential curves (chart 4 *B*) show that a higher peak of contraction speed is reached—frequently earlier—in the sympathectomized pupil than in the normal one. The descending branch of the C wave declines more rapidly than normal, and full contraction generally is reached earlier. The same is true of the D wave, which reaches a

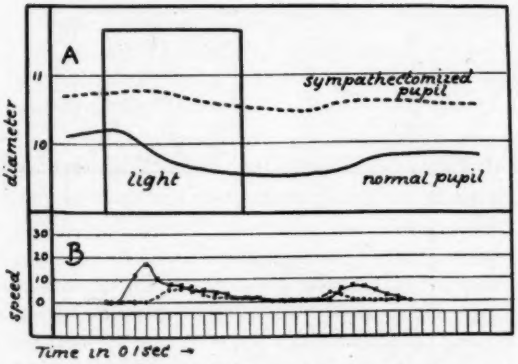

Chart 5.—Pupillogram (*A*) and differential curve (*B*) of the reaction to light in a highly excited cat with unilateral postganglionic sympathectomy and hypersensitivity to epinephrine.

A, anisocoria, of 0.7 mm., with the sympathectomized pupil the larger one. The reaction to light is greatly reduced in extent and speed on both sides, more so on the sympathectomized side.

B, differential curve of the sympathectomized pupil (broken line), showing an even greater reduction of C and D waves and a shift even farther to the right than that of the normal pupil (solid line).

somewhat higher peak faster than normal and then declines quickly. The E wave is highly reduced. The entire differential curve appears shifted toward the left.

Excitement, by strengthening the central sympathetic influence, counteracts the effect of sympathectomy; however, since the sympathetic tonus of the normal pupil is increased simultaneously to an even higher degree, the difference between the normal and the sympathectomized pupil continues to exist, and may even be accentuated. Excitement has more effect on the sympathectomized than on the normal pupil (chart 5 *A*) only in cats with postganglionic sympathectomy in which hyper-

sensitivity to epinephrine has developed. The sympathectomized pupil becomes even larger than the normal one, and its contraction to light even less extensive and slower than that of the normal pupil. In the differential curve (chart 5 *B*) the peaks of the C and D waves are even more reduced and delayed than those of the normal pupil.

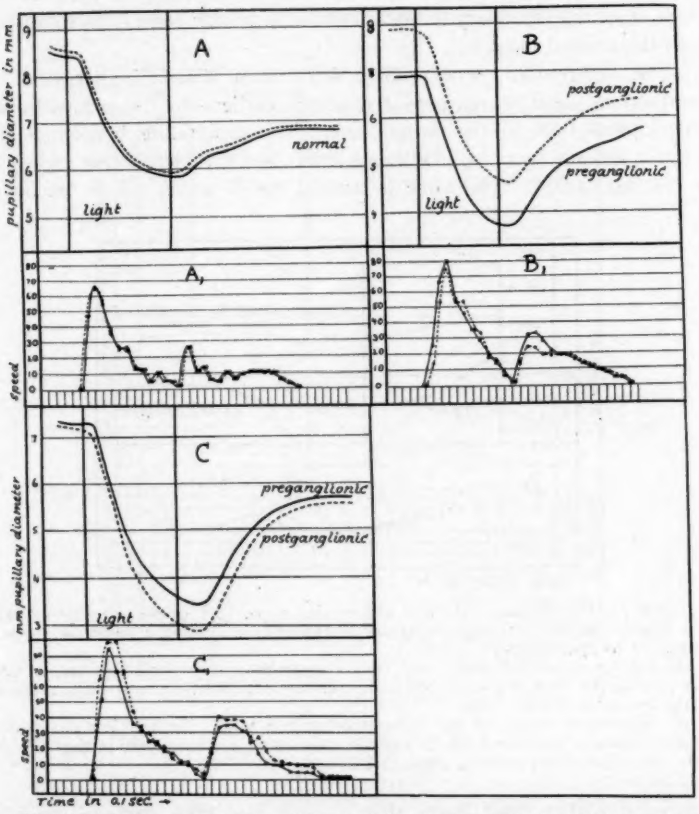

Chart 6.—Influence on the reaction to light of preganglionic (right) and postganglionic (left) sympathectomy performed in the same cat at the same time.

A and A_1, normal cat. The pupillogram and differential curves are identical on the two sides (right pupil, solid line; left pupil, dotted line).

B and B_1, early stage (twenty-four and forty-eight hours after operation). Contraction to light is slightly increased in the pupil (smaller) with preganglionic sympathectomy. The differential curve shows increase of C and D waves on this side.

C and C_1, later stage (seventy-two hours and subsequently), when the cat is calm. Reversal of conditions found in *B* has occurred. When the cat is excited, the condition described under *B* reappears.

3. *Influence of Postganglionic and Preganglionic Sympathectomy on the Reflex to Light in Cats.*—The differences in the effects of pregan-

glionic and postganglionic sympathectomy on the shape of the reflex to light were too slight to allow differentiation as long as we were dealing with different animals; possible differences were overshadowed by variations in the sympathetic-parasympathetic equilibrium from animal to animal and, in the same animal, from moment to moment, according to the changing emotional condition. Therefore we examined 3 cats, first while normal and then after sympathectomy, preganglionic on one side and postganglionic on the other side, was performed in one session. Thus we were able to compare, within the same reflex to light, the effect of preganglionic and postganglionic sympathectomy. Chart 6 shows light reflexes of a normal cat and those of the same cat twenty-four and seventy-nine hours after operation. While the direct and consensual reflexes to light were identical before the operation, differences appeared after operation. They are described as follows:

A. Early Stages Twenty-four and Forty-eight Hours After Operation (chart 6 *B*): 1. A slight anisocoria had developed, the pupil with postganglionic sympathectomy being about 0.33 mm. larger than the pupil with preganglionic sympathectomy.

2. The pupil with preganglionic sympathectomy reacted to light slightly more extensively than the pupil with postganglionic sympathectomy, while both reacted more extensively than before the operation.

3. The differential curves show that the preganglionic pupil with sympathectomy reacted faster in the ascending branch of both the C and the D waves, whereas the E waves are identical on the two sides. Both the C and the D waves are higher than prior to the operation; the E waves are reduced.

B. Later Stages, Seventy-Nine Hours After Operation (chart 6 *C*): Seventy-nine hours after operation we found that the anisocoria which had been in existence about thirty hours earlier was reversed when the animal was calm. The pupil with postganglionic sympathectomy had become smaller than the one with preganglionic sympathectomy. Its reaction to light was then more extensive than that of the other pupil. The differential curve showed the dynamic structure of the reactions also to be reversed, and that for the pupil with postganglionic sympathectomy had higher and earlier peaks of the C and D waves.

When the animal was excited, the condition returned to that shown in chart 6 *B*.

It is evident, therefore, that peripheral sympathectomy in cats—both preganglionic and postganglionic—changes the shape of the pupillary reflex to light in two respects: (*a*) It causes disinhibition of the contraction (C wave) and primary redilation (D wave), which go on at a higher speed than normal. This higher speed exists in all cases, although the extent of contraction is larger only in a certain number of cases.

(*b*) In all cases the secondary redilation phase (E wave) becomes very unstable and definitely diminished in its extent.

In cases of postganglionic sympathectomy in which hypersensitivity to epinephrine has developed in the denervated iris, excitement reverses these conditions.

4. *Influence of a Lesion of the Third Nerve on the Shape of the Pupillary Reflex to Light in Cats.*—Chart 7 shows the pupillogram of a cat one month after the ciliary ganglion of one side was slightly crushed.[3] After adaptation to dark red–infra-red illumination, the pupils were

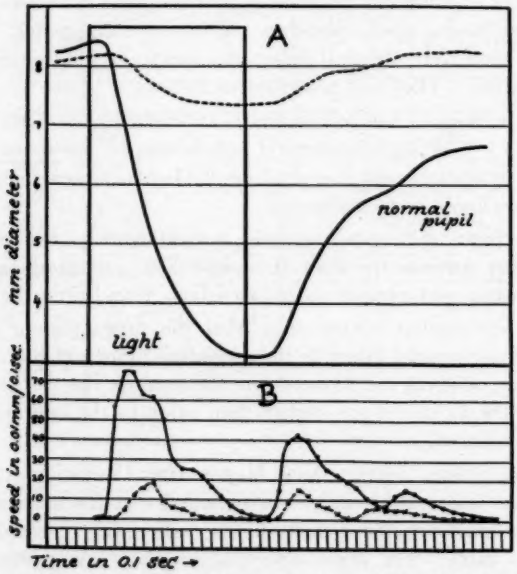

Chart 7.—Pupillogram (*A*) and differential curve (*B*) of the reaction to light in a cat in which one month before the ciliary ganglion had been crushed on one side.

(*A*) The reaction to light is sluggish and greatly reduced on the affected side. The latency period for contraction is increased.

(*B*) The C wave is greatly reduced and shifted to the right. D and E waves, also greatly reduced as compared with the normal, are less affected than the contraction wave.

roughly equal, at a diameter of about 8 mm. While the normal pupil showed an extensive contraction of about 5 mm., the pupil on the side of operation contracted sluggishly; the latency period was prolonged, and the extent of contraction was reduced to less than 1 mm. Redilation was also sluggish. The differential curve showed a low C wave with

3. This operation was performed by Dr. Andrew deRoetth Jr.

slowly ascending and descending branches. The D wave was slow and inextensive, and so was the E wave. Both pupillogram and differential curve are quite different from normal and are characterized by sluggishness and inextensiveness in all parts.

Since the partially parasympathectomized pupil contracted to a very slight extent (0.86 mm.), whereas the normal pupil contracted about 5 mm., dynamic contraction anisocoria of about 4 mm. developed.

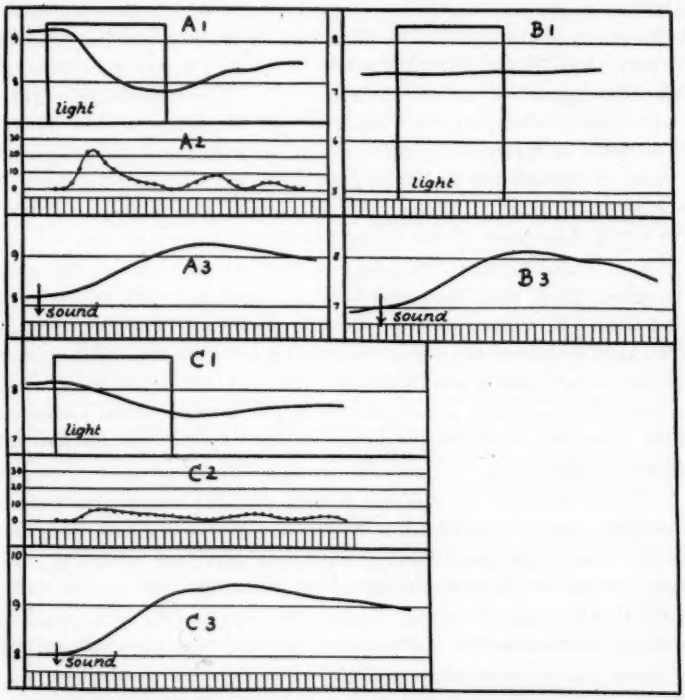

Chart 8.—Reactions to light and to sound stimuli in a rabbit before and after intraorbital injection of alcohol (0.3 cc. of 95 per cent alcohol).

A_1 and A_2, pupillogram and differential curve of the reaction to light in the normal rabbit.

A_3, reaction to sound in the normal rabbit.

B_1, two days after injection of alcohol. The reaction to light is abolished.

B_3, reaction to sound unimpaired.

C_1 and C_2, pupillogram and differential curve of the recovered reaction to light five weeks after injection of alcohol. The reaction to light is abnormally sluggish. The differential curve shows reduced peaks of movements and a shift to the right. C_3, normal reaction to sound.

5. *Influence of Partial Lesions of the Third Nerve on the Reflex to Light in Rabbits.*—This influence was also studied on 3 rabbits.

Three-tenths cubic centimeter of 95 per cent alcohol was injected into the region of the ciliary ganglion.[3] The animals were examined pupillographically before the injection and then were followed up from two days until five weeks after the injection. Reactions to light and to sensory stimuli were recorded (chart 8). It is interesting to note that by means of this operation it is possible to obtain absence of the reflex to light while the sympathetic reflex dilation is fully preserved (chart 8, B_1 and B_3).

It was found that the reflex to light recovered surprisingly fast; it was absent two days after the injection of alcohol but had returned a week after injection. However, it never recovered fully but remained sluggish (as shown in chart 8 C_1). The differential curve of this reaction is characteristic (chart 8 C_2). It shows a slow increase and decrease in speed of contraction. In order to reach the peak of the C wave, it needed 0.6 or 0.7 second (0.3 or 0.5 second before the operation); the relation between the contraction wave and the redilation wave changed in favor of the redilation wave.

While sympathectomy provokes a shift to the left of the entire differential curve, with decreased latency period and with higher peaks of the C and D waves occurring earlier, conditions involving the third nerve cause a shift of the entire differential curve to the right, with an increased latency period and decreased peaks of C and D waves occurring at a later time. This is a rule which we found in all animals observed and in man; we shall note it again in the experiments on monkeys (sections 9 and 10).

6. *Reflex to Light in Normal Monkeys.*—The reaction to light of the normal monkey consists of a contraction and redilation; in normal monkeys direct and consensual reactions to light are identical. The latency period for contraction lasts approximately 0.2 second and is slightly shorter than in man. No special experiments were made to determine the exact length of the latency period beyond the first decimal.

One of the foremost characteristics of the species of monkeys used in these experiments (Macaca mulatta) is their high excitability and the high variability, according to the emotional state of the animal, of both the shape and the extent of the pupillary reactions to light. In no other animal examined were we able to find such a variety of shapes so quickly following one another as we did in Macaca mulatta monkeys. All of them are the expression of the quickly changing degrees of excitement. Therefore Macaca mulatta monkeys proved to be particularly valuable for our purposes, since their reactions taught us to explain many reflex shapes which at first glance appeared unexplainable when we observed them as occasional phenomena in other animals, and especially in man. In general, redilation, as compared with the preceding

contraction, is more pronounced than in other animals observed and in man.

When the animal is sleepy (chart 9 *A*), the contraction lasts about one second or more. Primary and secondary contraction phases are well marked; the redilation appears faster than the contraction because high speeds are present longer in the redilation phase than in the contraction phase. The differential curve (chart 9 A_1) shows that the C wave reaches its peak quickly; this peak of contraction speed is neither very high nor long lasting and is followed by a period of gradually declining contraction speed (descending part of the C wave). The redilation wave is the expression of a forceful movement quickly reaching a relatively high peak of dilation speed, which is usually maintained for some time (several tenths of a second). The amplitude of the redilation wave frequently approaches, and may even surpass, that of the C wave, but D wave and E wave often merge and cannot be distinguished.

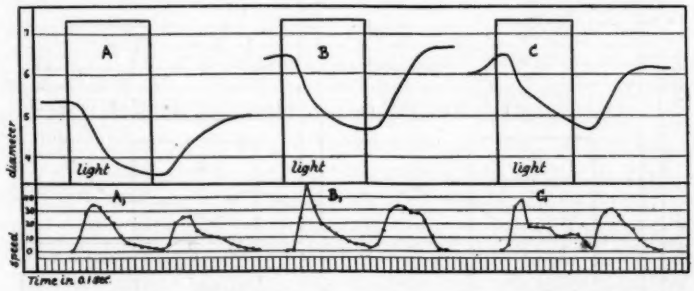

Chart 9.—Reactions to light in the normal monkey under the influence of increasing excitement. In the monkey the primary and secondary redilation phases merge and can rarely be distinguished. Therefore, in the monkey the term "D wave" applies to the combined D and E waves found in the rabbit, cat and man unless otherwise stated.

A, monkey sleepy; primary and secondary contraction phases well marked off; redilation vigorous. (A_1) The D wave is rather high in relation to the low C wave.

B, monkey mildly excited; contraction deeper; redilation more complete than in *A*. (B_1) Peaks of both C and D waves are increased.

C, monkey moderately excited. The primary and secondary contraction phases are so well marked off that the pupil deviates from its course of contraction at an angle of about 30 degrees. The secondary contraction phase is sluggish; redilation is vigorous. (C_1) The C wave has reached its rather low peak quickly. The descending branch of the C wave shows two phases: (1) a sudden drop from maximal contraction speed to about one-half the maximal speed, and (2) a period of very gradually declining contraction speed.

When the small animal is alert, but not excited (chart 9 *B*), the whole light reflex is increased; the contraction is deeper, and the redilation more complete and even faster than before. In the differential curve (chart 9 B_1), peaks for both C and D waves are higher than those shown in chart 9 *A*. As in chart 9 A_1, the E wave cannot be distinguished.

However, sympathetic activity is not absent in such cases. It manifests itself in the early and rapid decrease of contraction speed. The descending branch of the C wave shows two distinct phases: (1) a sudden drop from maximum to about one half to two thirds of the maximal contraction speed, followed by (2) a period of gradually declining speed of contraction.

When the animal is excited, one may get such pictures as those in charts 9 *C* and 10 *A*, *B*, *C*, and *E*, which show reactions to light as found

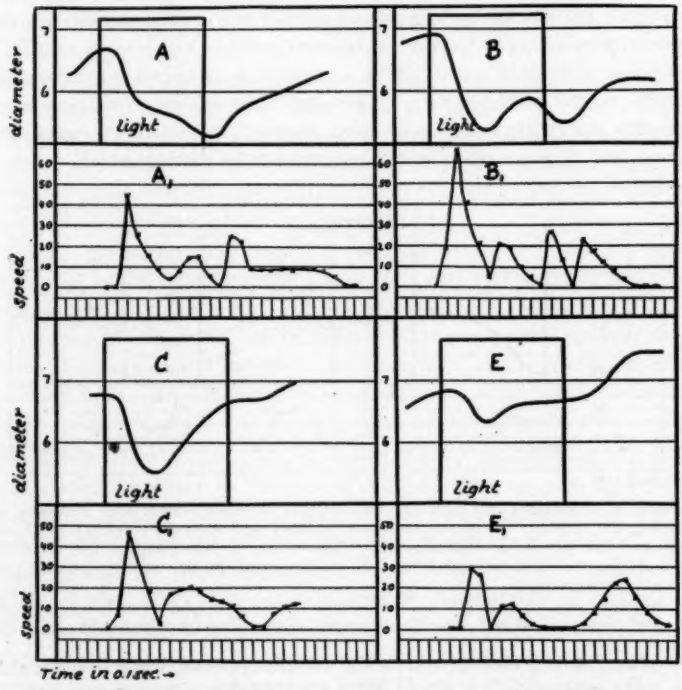

Chart 10.—Reaction to light in a normal monkey under the influence of mounting excitement.

(*A*) The contraction movement is, at the end of the primary contraction phase, interrupted by a moment of inhibited contraction.

(*B*) The moment of inhibited contraction is replaced by premature redilation (while the light stimulus is still in effect), followed by a second period of contraction and redilation with resulting W shape of the reaction to light.

(*C*) Premature redilation, no longer followed by a second period of contraction, leading to a V shape of the reaction to light.

(*E*) V shape of reaction to light with greatly reduced extent of contraction, found in highly excited monkeys.

in normal monkeys under the influence of increasing degrees of excitement. In the pupillogram of chart 9 *C* the first and second contraction

phases are so well marked off that the contraction curve, at the moment when the secondary phase starts, appears bent rather sharply, deviating from its former course at an angle of about 30 degrees. The sluggishness and reduced extent of the whole light reflex, particularly its low contraction speeds, as shown in the differential curve, seem to resemble the picture presented by the reaction to light in cases of parasympathetic lesion. However, differences exist:

1. No increase in the latency period for contraction is found.

2. The peak of the C wave is reached at the normal time of about 0.3 second (in parasympathetic lesions it is delayed up to 0.7 second).

3. The sudden drop in the first part of the descending branch of the C wave is well developed (not seen as an expression of parasympathetic lesions).

4. The D wave is normal in timing and extent (delayed and somewhat reduced in parasympathetic lesions).

With increasing excitement, the total extent of the contraction to light may become further reduced (chart 10 *A*). The bending at the beginning of the secondary contraction phase becomes even sharper (about 40 degrees). For a moment, the contraction movement almost comes to a standstill but is again resumed. In the pupillogram (chart 10 *A*) the moment of inhibited contraction appears as an upward bulging of the contraction curve; in the differential curve (chart 10 A_1) it is shown as a decrease in contraction speed to almost zero, followed by a second contraction wave (secondary C wave—wave of increased and decreased contraction speed).

As the animal's excitement further increases (chart 10 *B* and B_1), the moment of inhibited contraction gives way to a premature dilation, followed by a second period of contraction and redilation (W shape). Finally (chart 10 *C*, C_1 and *E*, E_1), in still stronger excitement, the secondary contraction movement of the W may be lost; the pupil dilates fully immediately after the first loss of contraction speed (V shape). In such cases, the pupil tends to become larger after the reaction to light than it had been before the contraction started.

7. Influence of Peripheral Sympathectomy on the Shape of the Reflex to Light in Monkeys.—If the peripheral sympathetic chain is interrupted, a disinhibition of the reflex to light takes place. The reaction to light becomes more extensive. The differential curve shows the increase in peaks of C and D waves and the shift to the left, as described in cats (section 2). Chart 11 shows, as a typical example, the pupillogram of a monkey in which the left superior cervical ganglion was removed. Anisocoria was present; the sympathectomized pupil was the smaller one. The animal had been asleep and was awakened (chart 11, *a*); approximately two seconds later a light stimulus was applied (*b-c*). At

the moment of awakening the monkey opened his eyes, and, after a latency period of about 0.2 second, the normal pupil performed an energetic dilation movement. The corresponding dilation in the sympathectomized pupil is not only reduced in extent but also different in its dynamic structure; the whole movement is slower and the peak of dilation speed reached at a later time (differential curve, chart 11 A_1).

The reflex to light (chart 11 B) shows a shape characteristic of mild excitement. The total contraction is slightly more extensive on the

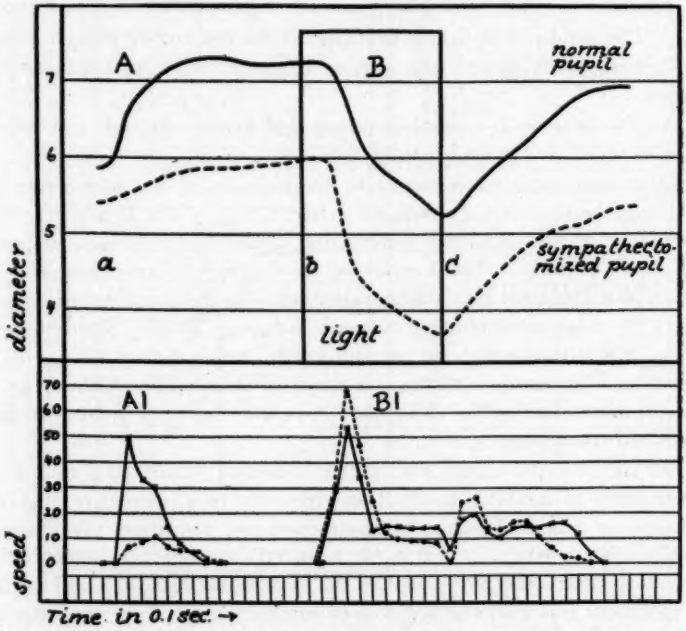

Chart 11.—Awakening and reaction to light in a monkey with unilateral cervical sympathectomy.

At *a*, the monkey, which had been sleeping, was awakened. Reflex dilation is greatly reduced and slow in the sympathectomized pupil. In the differential curve this is expressed by the low and delayed peak of dilation speed.

The reaction to light is increased in extent and speed on the sympathectomized side. The differential curve shows increased C and D waves, while the E wave is almost absent.

sympathectomized side than on the normal side. The differential curve (chart 11 B_1) shows a decidedly higher peak of the C wave in the sympathectomized pupil. The peak of the D wave is likewise higher on the sympathectomized side and is reached earlier; the E wave of the sympathectomized side is reduced as compared with the normal side.

It is interesting to compare the differential curve obtained from the dilation movement due to awakening with that obtained from the contraction movement of the reflex to light. In the normal pupil a striking similarity exists between the two curves, showing an increase and a decrease of speed of definite and similar proportions. In contrast to this, in the sympathectomized pupil the differential curve for reflex dilation shows disintegration both in extent and in timing (peak delayed, i. e., shift to the right), while the differential curve of the light reflex shows disinhibition with higher than normal peaks of C and D waves and a general shift to the left (increased speeds).

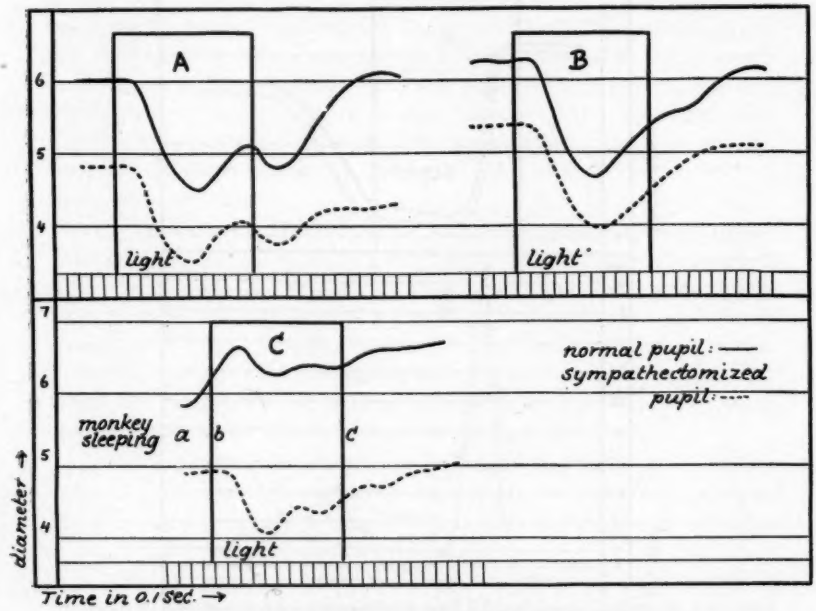

Chart 12.—Reactions to light of a monkey with unilateral cervical sympathectomy under the influence of mounting excitement. Peripheral sympathectomy has no influence on the formation of W and V shapes of the reaction to light.

Chart 12 shows the pupillary reactions of the same animal in conditions of greater excitement, producing W and V shapes of contraction.

From these curves it appears that the formation of W and V shapes of the reflex to light does not depend on impulses running over the peripheral sympathetic fibers, since they are well developed on both sides. Therefore, they must be the expression of a central nervous mechanism.

Active sympathetic impulses leading to pupillary dilation inhibit the contraction to light. This inhibition is diminished by peripheral sympa-

thectomy; chart 12 *C* illustrates this statement. The animal, which had been asleep, was awakened (at *a*); 0.3 second later (at *b*) a light stimulus was applied. Although the contraction to light of both pupils was inhibited, this effect was much more pronounced on the normal side. The contraction of the normal pupil was not only less extensive (about one half) than that of the sympathectomized pupil but was also delayed.

8. *Hypothalamic Lesions in Monkeys and Their Influence on the Shape of the Reflex to Light.*—When lesions are made in the posterior

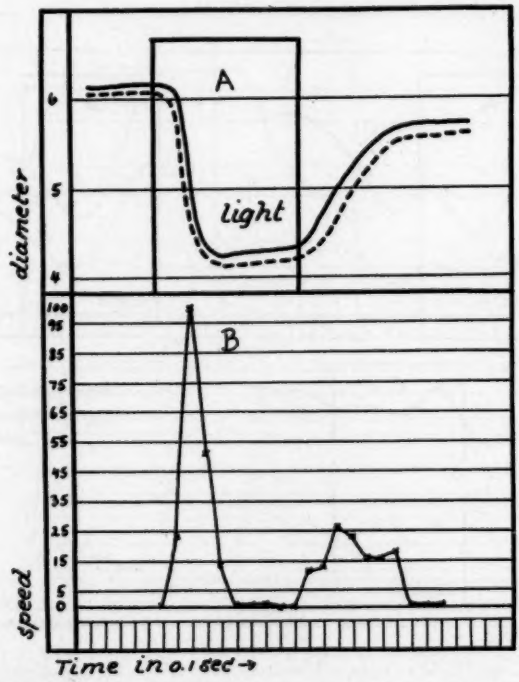

Chart 13.—Pupillogram and differential curve of a tonohaptic reaction to light in a monkey with a bilateral hypothalamic lesion.

The pupillogram shows (1) decreased latency period for contraction; (2) fast contraction; (3) full contraction, reached very soon after the beginning of the light stimulus and maintained until redilation sets in, and (4) vigorous redilation.

The differential curve shows an enormous peak of the C wave, followed by a fast drop to zero. The D wave is lower in relation to the C wave than in the normal monkey, but speed is maintained for a longer time than in the C wave.

hypothalamus in the manner previously described, the reaction of the pupil to light changes its shape (chart 13). This change of shape is very characteristic, although present to different degrees according to the localization of the lesion within the hypothalamus. Both pupils are

always involved in this change, even in cases in which the lesion is only on one side. The resulting shape of the reaction, called "tonohaptic,[3a]" is characterized by the following features:

(*a*) Anisocoria may or may not be present. If present, it is "static" in type.

(*b*) The latency period preceding contraction to light tends to be diminished. The contraction is performed at high speed; a high peak of contraction speed is generally reached after 0.2 or 0.3 second; the whole contraction movement quickly comes to an end (after about 0.6 to 0.7 second).

(*c*) When the contraction movement is completed, the reaction "hits the bottom"; that is, it has reached full contraction. This point is generally reached long before our standard light stimulus of one second's duration has come to an end; either the pupil remains immobile at this lowest point of contraction or a slight dilation starts while the light stimulus is still acting. After the light stimulus has come to an end, an energetic redilation movement starts either immediately or after several tenths of a second.

(*d*) The differential curve (chart 13 *B*) shows the C wave to ascend faster than normal and to reach a much higher peak of contraction speed. After the C wave has reached its peak, the contraction speed rapidly drops to zero. The differential curve remains close to zero until the D wave starts. The D wave is well developed; its peak (in contrast to that of normal monkeys) is considerably lower than that of the C wave, but speeds are maintained for a longer time than in the C wave. As in normal monkeys, an E wave cannot be distinguished.

(*e*) It is most significant that we no longer find the great variability —due to the constantly changing level of excitement—in extent and shape of the reaction to light which we found to be typical in normal monkeys of the species studied (Macaca mulatta).

Chart 14 *B* shows a series of typical reactions in a monkey with a bilateral lesion of the hypothalamus; chart 14 *A* shows normal reactions in the same monkey prior to the operation.

3a. The word "tonohaptic" was introduced by one of us (O. L.) many years ago, when, in collaboration with A. Westphal, (Lowenstein, O., and Westphal, A.: Experimentelle und klinische Studien zur Physiologie und Pathologie der Pupillenbewegungen mit besonderer Berücksichtigung der Schizophrenie, Berlin, S. Karger, 1933.) It was found that in certain cases of catatonia and encephalitic parkinsonism pupillary reactions to light occurred which were characterized by a very abrupt contraction movement, followed by a tonic-like state of constriction, which in turn gave way to an equally abrupt redilation movement. Pupillographically, the shape of the reflex resembled a trapezoid. This shape seemed to suggest that the iris adhered as long as possible to its condition of tonus in order to do the same —after an abrupt change—in the new condition of tonus (ἅπτω meaning to adhere).

The differences are striking; the normal reactions of chart 14 *A* have changed to the tonohaptic reactions of chart 14 *B*. While before operation a number of reactions to light present a picture of constant change, both in extent and in shape of the reaction, according to the changing emotional state of the animal, in the same animal after operation pupillary reactions to light go on with almost mechanical uniformity, showing little change in either extent or shape. Even a sound stimulus (chart 14 *B*, line 2) which causes the pupils to dilate extensively,

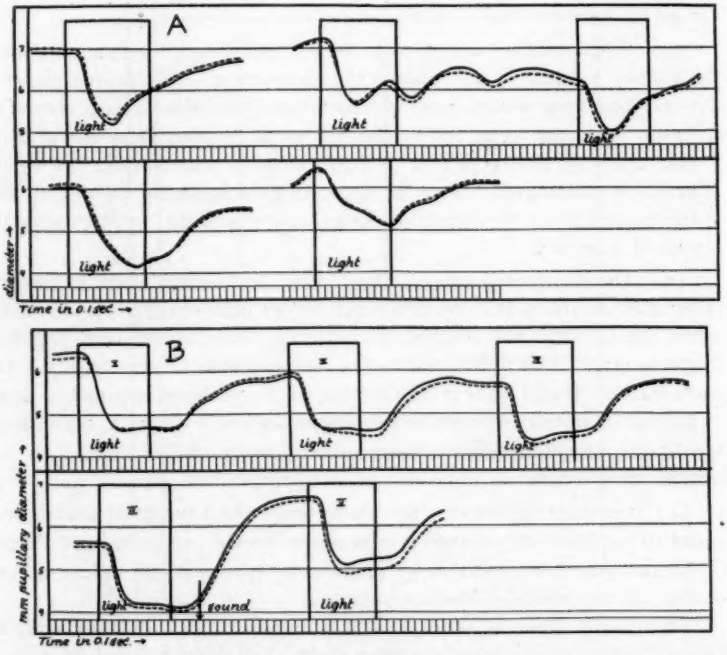

Chart 14.—*A*, a number of light reflexes in a normal monkey, showing the variability in shape and extent due to changing level of excitement.

B, series of light reflexes in the same monkey after bilateral hypothalamic lesion, showing the uniformity in shape and extent of the reactions. Despite a sound stimulus, which dilates both pupils vigorously, the shape of the following reaction to light shows little change.

thereby showing that it was an effective psychosensory stimulus, provokes only minor modifications of the following reaction to light. It does not change its tonohaptic character.

The case of chart 14 showed the effect of bilateral hypothalamic lesions. The same general features prevail in cases with unilateral lesions of the hypothalamus:

1. Anisocoria of static type may exist.

2. Tonohaptic reactions to light appear.

3. Psychosensory stimuli cause both pupils to dilate but have less than normal effect on the extent and shape of the subsequent reaction to light.

However, the effects of unilateral hypothalamic lesions are neither as pronounced nor as stable as those of bilateral hypothalamic lesions.

9. *Influence of Peripheral and Central (Hypothalamic) Sympathetic Lesions on the Shape of the Reflex to Light in Monkeys.*—If, in a monkey with unilateral peripheral sympathectomy a contralateral or a homolateral hypothalamic lesion is added, both pupils are affected. In such cases, then, one has a central condition affecting both pupils, in

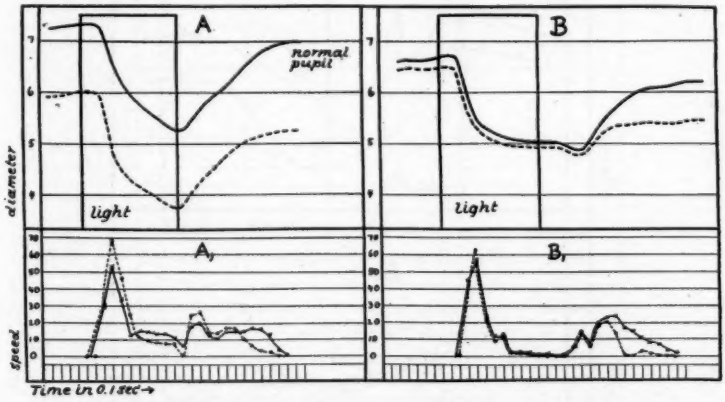

Chart 15.—Addition of a hypothalamic lesion in a monkey with unilateral cervical sympathectomy.

A, before the hypothalamic lesion. The picture is typical of unilateral peripheral sympathectomy: anisocoria, with the affected pupil the smaller one, and slightly increased reaction to light. A_1, differential curve, showing increased peaks of C and D waves and reduction of the E wave on the sympathectomized side.

B, after the hypothalamic lesion. Anisocoria due to peripheral sympathectomy has disappeared. The contraction and primary redilation are equal on the two sides, while the secondary redilation is missing on the side of the peripheral lesion.

addition to a peripheral condition affecting only one pupil. Pupillographic findings are as follows (chart 15):

1. On both sides occur tonohaptic reactions more or less pronounced and more or less constant, such as have already been described as the effect of a unilateral lesion of the hypothalamus (chart 15 *B*).

2. The static anisocoria which had been present prior to the hypothalamic lesion, and which was due to peripheral sympathectomy (chart 15 *A*) is reduced or has completely disappeared (chart 15 *B*).

3. Both pupils now (chart 15 *B*) contract equally to light (C waves are equal), while prior to the hypothalamic lesion (chart 15 *A*) the peripherally sympathectomized pupil had contracted more rapidly and extensively than the, at that time, normal one.

4. The primary redilation (D wave) is now equal on the two sides. Prior to the hypothalamic lesion it was stronger on the peripherally sympathectomized than on the normal side (chart 15 *A*).

5. The redilation wave is equal on the two sides in its ascending branch but comes to an abrupt end on the peripherally sympathectomized side, whereas it is maintained on the side without peripheral sympa-

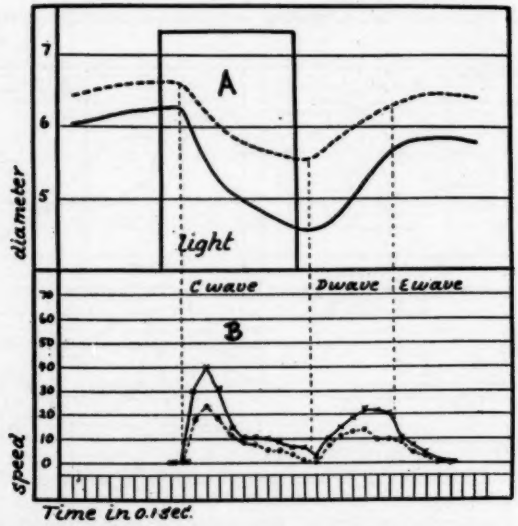

Chart 16.—Pupillogram and differential curve of the reaction to light of a monkey with unilateral lesion of the third nerve nucleus.

The affected pupil is the larger one. Reaction to light is reduced, causing dynamic contraction anisocoria. The differential curve shows reduced C and D waves, while secondary redilation is equal on the two sides.

thectomy, thus showing that the redilation wave in the monkey is a combination of D and E waves, such as are found in cats, rabbits and man. Owing to the absence of secondary redilation on the side with the peripheral lesion, dynamic redilation anisocoria develops.

10. *Influence of Lesions in the Third Nerve Nucleus on the Shape of the Reaction to Light in Monkeys.*—When the third nerve nucleus is completely destroyed, the pupil, of course, no longer reacts to light; but it may react to stimuli which provoke sympathetic reflex action, such as sound and pain, showing that sympathetic action and parasympathetic

action are not absolutely dependent on each other, although a quantitative interdependence exists. When, however, the third nerve nucleus is only partially destroyed, the reflex to light may, to a greater or less degree, be preserved. In such cases (chart 16) one finds anisocoria, except under the condition of darkness, with the pupil on the side of the lesion larger than that on the other side. When a light stimulus is applied to one of the eyes, both pupils react, one directly and the other indirectly, or consensually. The pupil of the normal side, of course, shows normal features, as already described. The pupil on the side of

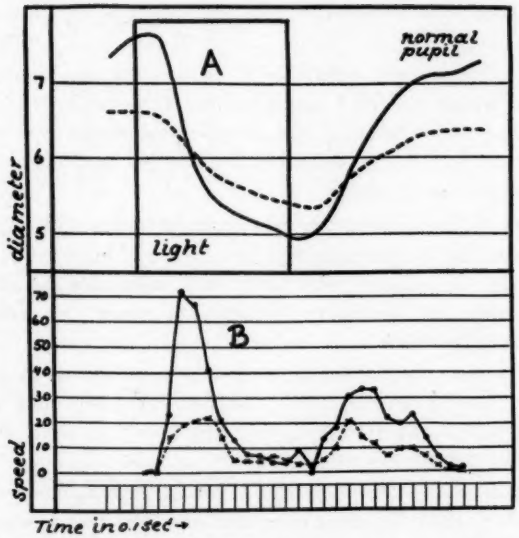

Chart 17.—Pupillogram and differential curve of the reaction to light in a monkey with unilateral lesion of the ciliary ganglion.

After dark adaptation, the affected pupil is smaller than the normal one. The reaction to light is reduced in both contraction and redilation. The differential curve shows decrease of peaks of the C and D waves and a shift to the right.

the lesion shows a sluggish and inextensive contraction and redilation. Anisocoria increases at the peak of contraction and decreases again when the pupils redilate. This type of anisocoria, "dynamic contraction anisocoria," is characteristic of lesions of the third nerve. In redilation, the anisocoria decreases as long as the primary redilation is going on but remains unchanged when the secondary redilation—which is predominantly due to peripheral sympathetic influences, and is therefore not disturbed on the side of the third nerve lesion—comes into play. The differential curve (chart 16 *B*) in such cases is drastically different from

the curves in cases of sympathetic lesions. The peaks of both C and D waves are low and delayed and appear shifted toward the right.

11. *Lesions in the Ciliary Ganglion and Their Influence on the Shape of the Reflex to Light in Monkeys.*—In monkeys, as in man, but not in cats, the sympathetic fibers run through the ciliary ganglion. Therefore, when one removes the ciliary ganglion in monkeys, one performs a complete denervation of the iris, including both the sympathetic and the parasympathetic nerve supply. Consequently, the pupil is mydriatic and does not react either to light or to sympathetic stimuli. When, however, the ciliary ganglion is only injured and is able to recover to a certain degree, one frequently finds such curves as those shown in chart 17.

The reaction to light (chart 17 *A*) shows features similar to those in cases in which the third nerve nucleus is injured: (*a*) prolonged latency period for contraction; (*b*) sluggish and inextensive contraction and redilation; (*c*) in the differential curve, low and delayed peaks of C and D waves (chart 17 *B*).

Contrary to our findings in cats or in monkeys with injured third nerve nucleus, the peripheral sympathetic factor is involved in the lesion. Consequently, the affected pupil, after dark adaptation, is smaller than the normal one, and secondary redilation (E wave), as well as active sympathetic reflex dilation, is impaired. Since the smaller pupil reacts less extensively to light than the normal one, anisocoria is reversed at the peak of contraction, the pupil with the lesion becoming the larger. This relation is again reversed when the pupils redilate, so that the affected pupil again is the smaller one.

12. *Influence of Sympathomimetic and Parasympathomimetic Drugs on the Shape of the Pupillary Reflex to Light.*—In the preceding article [1] we stated that in cats physostigminization diminished both sympathetic activity, i. e., reflexes to sensory stimuli, and parasympathetic activity, i. e., the reaction to light. Experiments on monkeys had similar results (chart 18).

When, in a normal monkey, 3 drops of a 1 per cent solution of physostigmine salicylate was instilled into the conjunctival sac, the pupils started to contract thirteen minutes after instillation of the first drop of the drug. After forty-three minutes a minimal diameter of 2.4 mm. was reached. Light stimuli applied at intervals during the period of contraction resulted in reactions to light which became increasingly sluggish and less extensive. The differential curves showed a progressive decrease and delay of peaks and a shift to the right.

When, on the other hand, cocaine (3 drops of a 1 per cent solution) was instilled into the conjunctival sac of a normal monkey, the pupil

dilated. Just as in the physostigminized pupil, the reactions to light and to sensory stimuli of the cocainized pupil decreased progressively while the sympathetic tonus increased; i. e., the pupil dilated. The differential curves showed, very similar to the results in the physostigminized pupil, decreased and delayed peaks of C and D waves (shift to the right).

Chart 19 shows the effect of increasing sympathetic tonus on parasympathetic reflex activity. The pupillary reflex to light was observed under the influence of cocaine and epinephrine. We used a monkey in which the superior cervical ganglion had been removed some time prior

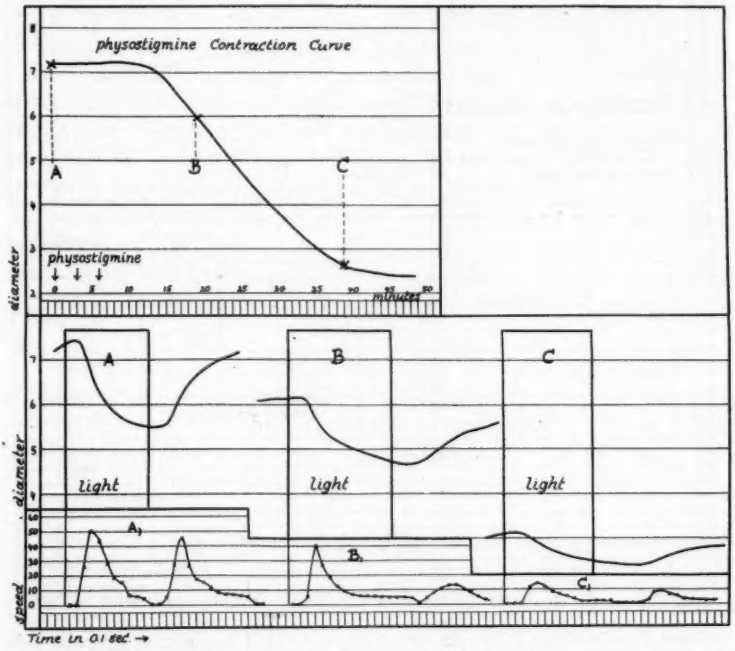

Chart 18.—Instillation of physostigmine salicylate (3 drops of a 1 per cent solution) into the conjunctival sac of a normal monkey and its effect on the reaction to light.

A, reaction to light before instillation of physostigmine (arrow indicates instillation of 1 drop).

B, reaction to light nineteen minutes after the instillation of the first drop of physostigmine. The reaction is less extensive and more sluggish than that shown in *A*. The differential curve shows decrease of peaks of the C and D waves.

C, reaction to light thirty-nine minutes after instillation of physostigmine, showing further decrease and slowing down of the reaction to light, with even lower and more delayed peaks of movements.

A_1, B_1 and C_1, differential curves for light reflexes.

to the experiment and hypersensitivity to epinephrine had developed in the denervated iris. Before instillation of cocaine (chart 19 *A*) the

monkey's reflex to light showed the familiar picture of unilateral postganglionic sympathectomy; the peaks of C and D waves were heightened, and the differential curve shifted to the left on the sympathectomized side. After instillation of cocaine into both conjunctival sacs, the normal pupil gradually dilated, while the sympathectomized pupil showed no effect. A light reflex, elicited thirty-six minutes after instillation of the first drop of cocaine, showed that the reaction of the sympathectomized pupil was unaltered (chart 19 *B*), whereas the dilated normal pupil,

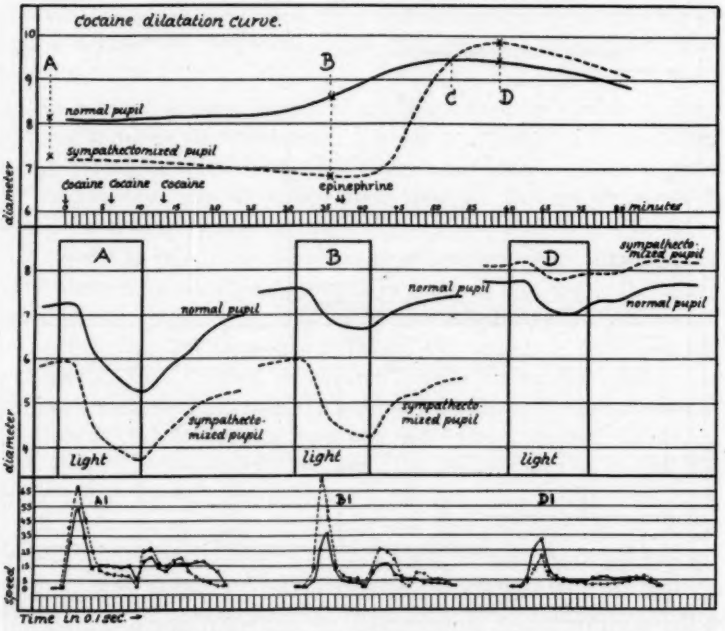

Chart 19.—Instillation of cocaine (1 per cent) and epinephrine hydrochloride (1:1,000) into the conjunctival sac of a monkey with unilateral cervical sympathectomy.

A, reaction to light without drugs, showing the typical picture of peripheral sympathectomy.

B, reaction to light thirty-six minutes after instillation of the first drop of cocaine. The normal pupil has dilated to 7.6 mm. Its reaction to light is reduced and slowed down, with decreased and delayed peaks of movements in the differential curve. The sympathectomized pupil is unaffected.

C, reaction to light twenty-three minutes after the instillation of epinephrine. The sympathectomized pupil now is the larger one. Its reaction to light is even less extensive and slower than that of the normal pupil. In the differential curve the peaks of the C and D waves are even more reduced and delayed.

after a prolonged latency period, reacted sluggishly and inextensively to light. Whereas the differential curve of the sympathectomized pupil was

unchanged, the normal pupil showed the peaks of C and D waves reduced and shifted to the right. Thirty-seven minutes after instillation of the first drop of cocaine, we added 2 drops of epinephrine hydrochloride (1:1,000) into each conjunctival sac. While the normal pupil was not affected, the sympathectomized pupil responded with a powerful dilation, causing the diameter of the sympathectomized pupil to reach (fifteen minutes after instillation of epinephrine, chart 19 *C*) and to exceed (eighteen minutes after instillation of epinephrine, chart 19 *D*) the diameter of the normal one. A light reaction elicited when both pupils were about equal in size resulted in identical pupillograms, as well as differential curves on the two sides. A light reflex elicited when the sympathectomized pupil had become larger than the normal one (chart 19 *D*) showed a reversal of the conditions found at *B*. The sympathectomized, hypersensitive pupil, now larger than the normal one, reacted even more sluggishly and inextensively than the normal one; in the differential curves of the sympathectomized pupil, C and D waves were even more reduced than those of the normal pupil.

This means that, in normal monkeys and cats, parasympathomimetic and sympathomimetic drugs increase parasympathetic and sympathetic tonus but diminish parasympathetic and sympathetic reflex activity, both in extent and in speed.

COMMENT

Pupillographic recordings of the reflex to light were studied in rabbits, cats and monkeys, both before and after experimental lesions at different levels of their sympathetic and parasympathetic control. The pupillographic curves show a variety of shapes; their dynamic characteristics become even more apparent when they are studied in the light of the differential curves.

Basically the pupillograms of the reflex to light and their differential curves show similar characteristics in all animals examined and, as may be added from our clinical pupillographic experience, in man as well.

The reflex to light in all species consists of a contraction and a redilation. The latency period for contraction lasts about 0.2 second, somewhat shorter in the monkey and longer in the rabbit. No special experiments were made to determine the exact time beyond the first decimal. The contraction movement consists of at least two phases, a fast, primary, and a slower, secondary phase. Redilation, likewise, consists of a faster, primary, and a slower, secondary, phase.

The differential curve derived from the original pupillogram of the reflex to light shows, in general, three different waves of increasing and decreasing speed of motion: a contraction wave (C wave), a primary redilation wave (D wave) and a secondary redilation wave (E wave). In the monkey, D and E waves frequently merge and can rarely be

distinguished. The ascending branch and peak of the C wave correspond to the primary contraction phase of the pupillogram; the descending branch corresponds to the secondary contraction phase. The D wave corresponds to the primary redilation phase, and the E wave, to the secondary redilation phase, of the pupillogram. All varieties of reflex shapes found in the pupillogram are reflected in the differential curves as quantitative differences of the C, D and E waves—their amplitude, length and shifting position on the time axis.

In all animals examined, the shape and extent of the reaction to light differ according to the emotional condition of the animal at the time when the light stimulus is applied. In highly excitable animals, such as Macaca mulatta monkeys, all possible variations of reflex shape and extent may be found in rapid succession; this is a physiologic expression of changing sympathetic tonus. As a general rule, a certain sympathetic tonus is necessary for the production of a normal parasympathetic pupillary reflex, i. e., the reflex to light. In case the optimal tonus is shifted by irritation or a lesion of the sympathetic centers or pathways, the pupillary reaction to light is changed in shape and/or reduced in extent.

In the preceding article [1] we were able to show that increase—for instance, by physostigminization—or decrease—for instance, by section of the third nerve—of parasympathetic tonus is unfavorable to the production of active sympathetic reflexes.

We therefore come to the general conclusion that in the dynamic sympathetic-parasympathetic equilibrium a certain relationship exists which is a prerequisite for the production of optimal autonomous reflex activity.

In spite of the similarity of the basic characteristics of pupillograms and their differential curves in all animals used, a number of stable relations exist, characteristic of the different species examined:

(*a*) Cats: When the animal is calm, the pupillogram of the reaction to light shows a block of redilation after contraction to light; this is reflected in the differential curve as a relatively high C wave and comparatively reduced D and E waves. When the animal is excited, the redilation block is replaced by a more or less complete inhibition of contraction. The degree of inhibition increases and decreases with the degree of excitement. The increase is reflected in the differential curve by reduced and delayed peaks of movement, with the C wave more affected than the dilation waves.

(*b*) Monkeys: When the animal is calm, the pupillogram of the reaction to light shows a relatively slow contraction and a forceful, rapid redilation. In the differential curve, the C wave reaches a relatively low

peak quickly; this is followed by a period of gradually declining contraction speed. In contrast to cats, the amplitude of the single dilation wave (merged D and E waves) approaches, and may even surpass, that of the C wave. When the animal is mildly excited, a strong inhibition of contraction sets in immediately after the primary contraction phase. In the differential curve this is expressed in the descending branch of the C wave as a sudden drop from maximal contraction speed to a value of about one-half the maximum, followed by a period of very gradually declining contraction speed. With increasing excitement the inhibition may cause a momentary standstill of contraction, or even a premature redilation, followed by a second period of contraction and redilation and leading to a W shape of the light reflex. In strong excitement this premature redilation is no longer followed by a secondary contraction and redilation, with a resulting V shape of the reaction to light, which diminishes in extent; in case of extreme excitement the reflex to light may be completely absent. It seems as though the W shape, and the V shape as well, have their origin in the fact that under the influence of excitement the sympathetic influence at the end of the primary contraction phase is stronger than the parasympathetic influence, and therefore reverses the direction of the movement from contraction to dilation. In the case of the W-shaped reflex the sympathetic control does not appear strong enough to maintain this reversed motion; in the case of the V-shaped reflex it seems able to do so. The V shape, therefore, is the expression of the stronger excitement; this concurs with the general behavior of the animal during the experiments. In another article, which will appear later, we shall show that the W and V shapes of the reaction to light appear not only as the expression of absolutely increased sympathetic tonus due to excitement but also as the expression of relatively increased sympathetic tonus due to parasympathetic insufficiency.

Since peripheral sympathectomy has no influence on the production of W and V shapes of the reaction to light, their foundation must be due to central mechanisms.

(*c*) Rabbits: As compared with cats and monkeys, rabbits generally show rather slow and inextensive reactions to light, with a longer latency period for contraction and, in the differential curves, lower peaks of movement. The reflex to light is easily blocked by excitement.

The immediately visible effect of preganglionic and postganglionic cervical sympathectomy is, of course, anisocoria, since the sympathectomized pupil contracts. The degree of anisocoria varies with the emotional condition of the animal. In a rabbit with preganglionic sympathectomy, and in postganglionic sympathectomy without hypersensitivity to epinephrine, excitement increases the anisocoria, since the

normal pupil dilates in response to excitement more than does the sympathectomized pupil. In a rabbit with postganglionic sympathectomy in which hypersensitivity to epinephrine has developed in the denervated iris, excitement decreases anisocoria, and may even reverse it, since in such cases the hypersensitive pupil dilates more than the normal one.

Peripheral sympathectomy results in a modification of the reaction to light. Contraction and primary redilation phases of the affected side are disinhibited, since the antagonistic sympathectic activity is weakened; therefore these movements go on at a higher speed than normal (higher peaks of C and D waves). Higher speeds exist in all cases, although the extent of contraction is larger only in a certain number. This is easily understood in the light of the fact aforestated, namely, that a certain optimal relationship between sympathetic and parasympathetic tonus is prerequisite for the development of an optimal reflex to light. In cases of preganglionic sympathectomy and of postganglionic sympathectomy without hypersensitivity to epinephrine, when the animal is calm and the sympathetic tonus of the normal pupil is optimal, the sympathectomized pupil reacts to light somewhat more quickly, the antagonistic sympathetic tonus is weakened and therefore its contraction is disinhibited; but since its sympathetic tonus is below optimum, the faster contraction of the sympathectomized pupil comes to an earlier end. The descending branch of the C wave drops faster, and the preexisting anisocoria diminishes at the peak of contraction. We call this anisocoria, "converging static anisocoria." If the sympathetic tonus of the normal pupil is below optimum—for instance, because the animal is sleepy or "fatigued" by repeated light stimuli—a similar condition prevails, inasmuch as the normal pupil is still nearer the optimum than the sympathectomized one. Therefore, anisocoria is again of the convergent type.

When the animal becomes excited, conditions are reversed. Now the sympathetic tonus of the normal pupil rises above the optimum, while the tonus of the peripherally sympathectomized pupil approaches the optimum. The reflex to light of the normal pupil becomes inhibited, and that of the sympathectomized pupil becomes more extensive. The preexisting anisocoria increases during contraction to light. The difference of contractions becomes more pronounced while the animal becomes more excited, thereby increasing the "divergent [dynamic] contraction anisocoria." This is easily understood because increasing excitement increases the sympathetic tonus more on the normal side than on the peripherally sympathectomized side; the stronger sympathetic tonus inhibits the contraction to light relatively more than does the weaker tonus of the sympathectomized pupil.

The effect on the reaction to light of postganglionic sympathectomy with hypersensitivity to epinephrine is identical with that of preganglionic

sympathectomy as long as the animal is calm. As soon as it becomes excited, the condition reverses, because in these cases the hypersensitive pupil, which has become larger than the normal pupil, is even more inhibited against contraction to light than is the normal pupil. The C and D waves are even more decreased and delayed.

In all cases of peripheral sympathectomy the secondary redilation phase (E wave) becomes very unstable and definitely reduced in extent.

However, the differences in the effect of preganglionic and postganglionic sympathectomy are slight; we were able to demonstrate them only within the same reflex to light in a cat with preganglionic sympathectomy on one side and postganglionic sympathectomy on the other side, by comparing the direct with the consensual reaction.

Sympathectomy increases the C and D waves; this indicates that, normally, they are inhibited by impulses running over the peripheral sympathetic fibers, while they are due to a process of innervation and relaxation of the parasympathetic fibers mediated through the nucleus of the third nerve. The fact that after peripheral sympathectomy the E wave is almost absent means that its presence is due primarily to an active sympathetic reflex through the cervical sympathetic chain.

If the sympathetic lesion is made at the level of the posterior hypothalamus, a drastic change in the shape of the reaction to light takes place. The tendencies shown as results of peripheral sympathectomy are greatly exaggerated, and a new reflex shape appears: the tonohaptic reflex to light. It is characterized by (*a*) reduction in pupillary diameter; (*b*) reduced latency period for contraction; (*c*) a fast contraction movement performed almost exclusively during the primary contraction phase and leading to full contraction; (*d*) immobility of the pupil at full contraction until, some time after the light stimulus comes to an end, redilation sets in; (*e*) redilation in one swift motion; (*f*) in the differential curve, a greatly increased peak of the C wave—much more than in peripheral sympathectomy—the descending branch of the C wave dropping quickly to zero and remaining near zero until redilation sets in. The D wave is well developed.

Prior to the hypothalamic lesion, the shape and extent of the pupillary reflex to light varied constantly; we have already stated that this was due to the constantly changing level of excitement of the highly excitable monkeys used. It is important to note that this variability of the reflex is lost after the operation, when the pupillary reactions to a series of light stimuli go on with almost mechanical uniformity and show little change in either extent or shape. Psychosensory dilation reflexes are fully preserved. We therefore conclude that the inhibition of the reflex to light which is produced by excitement and which, by the different degrees of excitement, creates the great variety of reflex shapes in normal

animals, is not performed over the peripheral sympathetic pathways. It must be performed over the posterior hypothalamic centers (or pathways), which were destroyed in our experiments and over which the activity of the third nerve is inhibited.

Tonohaptic reactions and the mechanical uniformity of their shapes were first observed in man in 1933 by Lowenstein and Westphal [4] in clinical pupillographic observations on patients with catatonia.

Central sympathetic impulses inhibiting the third nerve nucleus, therefore, have a much greater influence on the shape of the reaction to light than impulses traveling over the peripheral sympathetic chain; however, the secondary redilation phase, which is preserved in cases of lesions of the posterior hypothalamus, depends mainly on impulses running over the peripheral sympathetic fibers.

Anisocoria due to peripheral sympathectomy tends to disappear when a hypothalamic lesion is added to the peripheral lesion; both pupils then become even smaller than the pupil on the sympathectomized side had been prior to the hypothalamic lesion. In these cases, however, the anisocoria does not disappear completely but becomes latent; it reappears during redilation after contraction to light, and this is due to the absence of the E wave on the side of the peripheral lesion. It also reappears during active sympathetic reflex dilation in response to sensory stimuli. This leads to the conclusion that in the hypothalamus of Macaca mulatta monkeys those sympathetic impulses which run over the peripheral sympathetic fibers and those which run over the so-called central inhibition pathways to the third nerve nucleus are separated.

The effects of lesions in the posterior hypothalmus are most pronounced in cases in which the lesions were produced bilaterally; however, they were present bilaterally also in cases of unilateral hypothalmic lesion, although less constantly and, frequently, to a less degree. In these cases tonohaptic reactions were sometimes latent; that is, they did not always appear at the first stimulation by light, but appeared only on repetition of light stimulation at the second or third reaction. This experimental fact is in agreement with clinical observations in cases of diencephalic lesions. The phenomenon is frequently seen in the initial stages of diseases in which fully developed tonohaptic reactions appear at a later stage.[2b, c]

Damage to the parasympathetic centers or pathways has effects different from those produced by impairment of the sympathetic centers or pathways.

4. Lowenstein, O., and Westphal, A.: Experimentelle und klinische Studien zur Physiologie und Pathologie der Pupillenbewegungen, mit besonderer Berücksichtigung der Schizophrenie, Berlin, S. Karger, 1933.

Nonirritative, incomplete lesions in the nucleus of the third nerve of the monkey result in (*a*) dilatation of the pupil on the side of the lesion, and thereby anisocoria, except under the condition of darkness, when the pupils become roughly equal in size; (*b*) an increased latency period for contraction; (*c*) sluggish and inextensive contraction and redilation to light, leading to dynamic contraction anisocoria, a condition reflected in the differential curve by delayed C and D waves of low amplitude; (*d*) an unimpaired E wave, as well as sympathetic reflex dilation in response to sensory stimuli.

Partial lesion of the ciliary ganglion in cats causes changes identical with those described as the effect of damage of the third nerve nucleus in the monkey; this is understandable from the anatomic fact that in cats, in contrast to monkeys and man, the peripheral sympathetic fibers do not traverse the ciliary ganglion; therefore, when the ciliary ganglion is damaged in cats, only parasympathetic fibers are impaired.

Partial damage to the ciliary ganglion in monkeys results in features of the reflex to light which are similar to those found after partial lesion of the third nerve nucleus. However, since in monkeys the sympathetic fibers run through the ciliary ganglion, the affected pupil, after dark adaptation, is smaller than the normal one; the secondary redilation after contraction to light (E wave), as well as sympathetic reflex dilation in response to sensory stimuli, is reduced or absent.

Partial damage to the ciliary ganglion in rabbits, produced by intra-orbital injection of alcohol, shows the same features of sluggishness and inextensiveness and the same reduction of C and D waves of the differential curve as described in other species. Sympathetic reflex dilation in response to sensory stimuli may be unimpaired.

In normal animals, when parasympathomimetic drugs, such as physostigmine, or sympathomimetic drugs, such as cocaine, were applied, the parasympathetic-sympathetic dynamic equilibrium was shifted to the one or the other side and, according to the general conclusions already drawn, optimal, or even normal, pupillary reflex activity was no longer to be expected. This was realized in our experiences. Pupillary reactions to light and sensory stimuli become progressively sluggish and inextensive as the sympathetic or parasympathetic tonus increases and finally are abolished when the tonus of either side has reached extreme values.

In cases of physostigminization and cocainization, reaction shapes are found which otherwise are seen only in conditions of the third nerve. In the case of cocainization, the explanation has probably to be sought in the fact that strengthening of the sympathetic tonus produces a relative weaking of the third nerve. This phenomenon—relative weakening of the third nerve—was previously found in man and was called "pseudo-

oculomotor phenomenon" (Lowenstein, Franceschetti). In the case of physostigminization, the explanation probably lies in the fact that the condition symptomatically resembles a supranuclear lesion of the third nerve such as the Argyll Robertson phenomenon.

The forces causing the movements of contraction (C wave) and primary redilation (D wave) are delivered by the parasympathetic system; the relatively small forces responsible for the formation of the E wave are delivered by the sympathetic system. But the dynamic structure of parasympathetic reflex activity, i. e., the reflex to light, and of sympathetic reflex activity as well, i. e., the psychosensory dilation reflex, depends on the strength, duration and timing of coinciding sympathetic and parasympathetic impulses. As far as the light reflex of the pupil is concerned, it may be worded this way: The parasympathetic factor is essential for the light reflex to come into appearance; the sympathetic factor determines its shape. It becomes clear to which degree this statement is true when the tonohaptic reflex, which appears after a hypothalamic lesion is set, is compared with the reflex to light prior to the operation.

The detailed analysis of the pupillary reflex to light was based on its experimental symptomatology, which led to the assumption of a reciprocal relation (Sherrington) between sympathetic and parasympathetic innervation. Since, in spite of anatomic differences, this relation is basically identical in all species examined, a priori, the supposition appears likely that its main functional manifestations are, *mutatis mutandis,* the same also in man.

The mutual role of the sympathetic and the parasympathetic innervation in the shaping of the pupillary reflex to light in man was analyzed and described in a former publication.[5] It was very similar to, if not identical with, the relation as detected in monkeys, cats and rabbits. On the other hand, all pupillographic syndromes produced by experimental lesions in animals were observed in man as clinical manifestations in pathologic processes of corresponding site.[6]

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5. Lowenstein and Levine.[2a] Lowenstein, O., and Givner, I.: Cyclic Oculomotor Paralysis (Spasmus Mobilis Oculomotorius), Arch. Ophth. **28**:821-833 (Nov.) 1942.

6. Lowenstein, O.: Clinical Diagnosis of Disturbances of the Central Sympathetic System by Means of Pupillography, Arch. Neurol. & Psychiat. **55**:682-684 (June) 1946. Lowenstein, O., and Friedman, E. D.: Pupillographic Studies: I. Present State of Pupillography: Its Method and Diagnostic Significance, Arch. Ophth. **27**:969-993 (May) 1942; Adie's Syndrome (Pupillotonic Pseudotabes), ibid. **28**:1042-1068 (Dec.) 1942. Lowenstein, O.: Les troubles du réflexe pupillaire à lumière dans les affections syphilitiques du système nerveux central, Paris, Gaston Doin & Cie, 1939.

Cortical factors which, possibly, contribute to the integration of the normal reflex shape, and which may manifest themselves in a disintegration of pupillary functions if cortical lesions are set, are not included in this paper.

CONCLUSIONS

1. As shown by means of pupillographic experiments on monkeys, cats and rabbits, a certain relationship exists in the dynamic sympathetic-parasympathetic equilibrium which is a prerequisite for the production of optimal autonomous reflex activity. Deviations from the optimal sympathetic-parasympathetic relation, in favor or disfavor of either factor, disinhibit or inhibit autonomous reflex activity and, under extreme conditions, abolish it. This statement includes parasympathetic reflexes, i. e., the pupillary reflex to light, and sympathetic reflexes, i. e., the psychosensory dilatation reflex, and is in agreement with previously published results of experiments on man.

2. In all species mentioned the pupillary reflex to light consists of the same elements. The contraction movement consists of at least two phases, a fast, primary, and a slower, secondary, phase. Redilation also consists of two phases, a faster, primary, and a slower, secondary, phase.

3. Differential analysis of the pupillographic curve of the reflex to light shows, in general, three waves of increasing and decreasing speed of motion: a contraction wave (C wave), a primary redilation wave (D wave) and a secondary redilation wave (E wave).

The ascending branch and peak of the C wave correspond to the primary contraction phase of the pupillogram; the descending branch corresponds to the secondary contraction phase. The D wave corresponds to the primary redilation phase, and the E wave, to the secondary redilation phase, of the pupillogram.

4. The ascending branch and peak of the C wave are primarily due to parasympathetic activity; the descending branch of the C wave is due to parasympathetic reflex activity, damped by increasing antagonistic sympathetic influence, predominantly central but also peripheral. The D wave is predominantly due to parasympathetic relaxation, while the E wave depends mainly on impulses running over the peripheral sympathetic pathways.

All varieties of reflex shapes are reflected in the differential curves as quantitative differences of the C, D and E waves—their height, length and shifting position on the time axis. A number of stable relations characteristic of the different species examined exist and are described.

5. The dynamic structure of the pupillary reflex to light depends on the strength, duration and timing of coinciding sympathetic and parasympathetic impulses. The parasympathetic factor is essential for the

light reflex to come into appearance; the sympathetic factor determines its shape. Variations of either factor at different neurologic levels have the following effects:

A. Variations of the sympathetic factor

I. Strengthening of central sympathetic activity by excitement in normal animals of all species examined

(1) Development of W shapes
(2) Development of V shapes
(3) Inhibition of contraction, which becomes inextensive and sluggish
(4) Absence of contraction

II. Strengthening of sympathetic influences by sympathomimetic drugs

Contraction sluggish and inextensive (pseudooculomotor phenomenon)

III. Weakening of sympathetic influences by peripheral sympathectomy in all species examined

(1) Disinhibition of contraction with increase of speed and possible increase of extent
(2) C and D waves appearing earlier (shifted to the left) and higher
(3) E wave diminished or absent

IV. Weakening of sympathetic influences at level of posterior hypothalamus in monkeys

(1) Bilateral tonohaptic reaction shape with earlier and heightened peak of C wave, which drops quickly to zero, and well developed D wave (shifting to left)
(2) Loss of variability of shape and extent which is normally present
(3) Unimpaired secondary redilation phase
(4) Preexisting anisocoria may become latent

In cases with unilateral lesions, the tonohaptic reaction type may be latent.

B. Variations of the parasympathetic factor

I. Weakening of the parasympathetic tonus by lesions at two levels

(*a*) Nonirritative, incomplete lesion of third nerve nulceus in all species examined

(1) Contraction and redilation sluggish and inextensive
(2) Latency period increased
(3) C and D waves low and delayed (shifted to the right)

(b) Partial, nonirritative lesion of ciliary ganglion

(1) In cats and rabbits

Reaction like that to I (a)

(2) In monkeys and man

(a') Reaction like that to I (a)

(b') E wave absent

II. Strengthening of parasympathetic factor by parasympathomimetic drugs (or irritative lesion of third nerve nucleus or ciliary ganglion):

(1) Contraction sluggish, inextensive

(2) C and D waves low and delayed (shifted to the right)

6. The various reaction shapes as conditioned by irritation or lesions at various levels of sympathetic or parasympathetic control are frequently accompanied with various types of anisocoria, the symptoms and genesis of which are described in detail.

7. All pupillographic syndromes produced by experimental lesions in animals are observed in man as clinical manifestations of pathologic processes of corresponding sites.

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SOME DATA CONCERNING THE GROWTH AND DEVELOPMENT OF THE CEREBRAL CORTEX IN MAN

II. Postnatal Growth Changes in the Cortical Surface Area

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AS WAS indicated in an earlier publication,[1] this study of the growth and development of the nervous system was initiated by the late Dr. T. Wingate Todd as a portion of a general program for the study of growth and development. Many factors have contributed to delay the publication of the available data, and the present study is the second of the series. The present communication concerns the growth of the cerebrum as it is reflected in the changes in surface area of the free, or visible, cortex. The cortical surface area was determined for 14 brains, of persons ranging in age from 3 weeks to 24 years, and figures were obtained for each lobe of the two hemispheres. In no case was the brain used when there was any indication of a primary disease process affecting the nervous system. For the purpose of measurement, the various lobes of the brain were identified in the same manner as that employed in the first paper of this series.[1] While the sample is too small to permit the correction of individual variations, certain aspects of the growth process are apparent and warrant publication.

METHOD

The method consisted in covering the gyri with 24 carat gold leaf of 0.00571275 cm. (0.0025 inch) thickness. The surface area was obtained by dividing the weight of the gold leaf used by 19.32, the specific gravity of the gold. The result, which was the cubic centimeters of gold used, was divided by the thickness of the gold leaf, and the area was thus obtained. In actual practice, however, it was necessary only to multiply the weight of the gold leaf by the constant 9.06.

$$\text{Area} = \frac{\dfrac{\text{Weight of gold used}}{\text{Specific gravity of gold used}}}{\text{Thickness of gold}}$$

Specific gravity of gold used = 19.32
Thickness of gold leaf = 0.00571275 cm.
Area = Weight of gold used × K
K = 9.06

From the Anatomical Laboratories, Western Reserve University School of Medicine, Cleveland.

1. Turner, O. A.: Growth and Development of the Cerebral Cortical Pattern in Man, Arch. Neurol. & Psychiat. **59**:1 (Jan.) 1948.

REVIEW OF LITERATURE

Because of the many methods employed in the study of the growth of the cerebral cortex, correlation of the various methods obtained becomes difficult, and at times impossible. From the standpoint of growth changes there have been relatively few investigations employing direct measurement. No attempt will be made to review the literature comprehensively, and reference will be made to only a few pertinent studies.

Determination of the extent of cortical surface was first carried out by R. Wagner in 1862,[2] and the work was continued by H. Wagner [3]

TABLE 1.—*Summary of Data Collected from the Literature Concerning Cortical Surface Area in Man*

Author	Method of Determination	Total Surface (Sq. Mm.)	Visible Surface (Sq. Mm.)	Visible/ Total
Wagner [3] (1864)	Gold leaf method; sulci measured directly	221,005	.....	.....
Baillarger [7]	Cortex dissected and unfolded, measured directly	170,000	.....	.....
Calori, cited in Quain's Anatomy, 1909, vol. 3, pt. 1, p. 341	Determinations on 41 brains	Males Brachycephalic..247,773 Dolichocephalic..230,212	.....	.....
		Female Brachycephalic..211,701 Dolichocephalic..198,210	.....	.....
Danilewsky, cited by Kraus and others [10]	Weight of brain; specific gravity of gray and white matter, etc.	169,200	.....	.....
Donaldson, H. H.: Am. J. Psychol. 3:296, 1890-1891	Calculated	200,000	.....	1:3
Henneberg [11] (1910)	Sections 1 cm. thick cut from sulci, covered with paper	226,200	77,000	1:2.94
Kraus, Davidson and Weil [10] (1928)	Serial sections projected; planimetric determinations	289,540	63,918	1:4.53

in 1864, both using the gold leaf technic. Jensen [4] used the same technic but employed tinfoil in 5 mm. squares, instead of the gold leaf employed by Wagner. The results of these studies are contained in table 1.

Anton,[5] in 1901, determined the area of the cerebral cortex by means of serial frontal sections, which were measured with a planimeter. The

2. Wagner, R.: Vorstudien einer wissenschaftlichen Morphologie und Physiologie des menschlichen Gehirns als Seelenorgan, 1862; cited by Kraus, Davidson and Weil.[10]

3. Wagner, H.: Massbestimmung der Oberflache des grossen Gehirns, Inaug. Dissertation, Göttingen, 1864; cited by Kraus, Davidson and Weil.[10]

4. Jensen, J.: Untersuchungen über die Beziehungen zwischen Grosshirn und Geistesstörung an sechs Gehirn geisteskranker Individuen, Arch. f. Psychiat., 1875, vol. 5.

5. Anton: Gehirnvermessung mittels des Kompensations Polar Planimeter, Wien. klin. Wchnschr. **46**:1263, 1903; cited by Kraus, Davidson and Weil.[10]

same method was used by Yager [6] in 1915. Baillarger [7] dissected and unfolded the cortex, taking direct measurements, while Paulier,[8] in 1892, used the same method as Wagner.

In 1927 Kraus and Ditto [9] devised a method for the measurement of cortical surface area by the use of serial sections, while Kraus, Davidson and Weil [10] in 1928 published a discussion of the technical difficulties involved in the measurement of cortical surface area. The determination of total and visible cerebral surface by Kraus and Ditto [9] gave figures somewhat larger than those obtained by Henneberg,[11] Wagner [8] and others (table 1). These authors found the total surface of the cerebral cortex to be 2,895.4 sq. cm. and the visible, or free, cortical surface to be 639.18 sq. cm. The ratio of total to visible surface of the cerebral cortex was 4.53:1. These figures take into account the slant, or angulation, of the various sections, which were cut at a thickness of 100 microns, and also allow for shrinkage. Hesdorffer and Scammon [12] investigated the growth changes of the cerebrum in terms of surface area. These investigations included the changes in the surface area of the cerebrum through a portion of the developmental period from the fourth fetal, or lunar, month of prenatal life to the second postnatal year and into maturity (table 2). The method consisted of sectioning formaldehyde-fixed brains enclosed in a matrix and determining the area by measuring the outline of sections and multiplying the reading by the thickness of the individual sections of the brain. Their results seemed to indicate three stages in the growth process with respect to the "total" cerebral surface. There was a very rapid increase in the fourth lunar month, although the material employed was too limited to indicate any greater, or even regular, increase in the fifth or sixth month. In the seventh and eighth lunar months, however, there was evidence of a very vigorous increase in total surface of the cerebrum, and there was an even greater growth period between the eighth lunar month and birth. In the postnatal life, there seemed to be a pronounced absolute, although not relative,

6. Yager: Inhaltsberechnung der Rindensubstanz, Arch. f. Psychiat. **54**:261, 1914.

7. Baillarger, J. G. F.: Cited in Quain's Anatomy, 1909, vol. 3, pt. 1, p. 341.

8. Paulier, A. B.: Recherches sur la notion de surface en anatomie. Determination de la surface du cerveau, Paris, 1892; cited in Quain's Anatomy, 1909, vol. 3, pt. 1, p. 341.

9. Kraus, W. M., and Ditto, M. W.: A Method for Measuring the Cerebral and Cerebellar Cortical Surfaces, Arch. Neurol. & Psychiat. **17**:193 (Feb.) 1927.

10. Kraus, W. M.; Davidson, C., and Weil, A.: The Measure of Cortical Surface, Arch. Neurol. & Psychiat. **19**:454 (March) 1928.

11. Henneberg, L.: Messung der Oberflächenausdehnung der Grosshirnrinde, J. f. Psychiat. u. Neurol. **17**:145, 1910.

12. Hesdorffer, M. B., and Scammon, R. E.: Observations of Human Cerebral Surface, Proc. Soc. Exper. Biol. & Med. **33**:415, 1935.

increase in infancy and very early childhood, but there was comparatively little, if any, increase after the latter period. These investigators found that the total surface of the cerebrum more than doubled in postnatal life. The free cerebral surface followed much the same pattern as the total surface until about the eighth lunar month, but the increase between this time and the age of 2 years, while striking, was much less rapid.

The authors regarded the interval from the sixth lunar month to some time in the second postnatal year as the period of rapid absolute increase in cortical surface, with the peak of most noticeable growth and total surface area in the last trimester of fetal life. These observations seem to be in accord with the purely morphologic observations on the time and extent of formation of the cerebral sulci in man.[1]

Woollard,[13] in studying the growth of the brain of the Australian aboriginal, found that there was a precocious development of the occipital

TABLE 2.—*Growth of Cerebral Surface**

Age	Total (Sq. Cm.)	Visible/Free Cerebral Surface (Sq. Cm.)
Newborn (average of 2)	697.75	230.5
2 mo.	724.10	249.9
4 mo.	954.1	333.2
5.3 mo.	944.1	294.8
2 yr.	1,666.4	457.3
26 yr.	1,635.3	552.9
44 yr.	1,610.1	568.7
49 yr.	1,468.7	523.1
Adult (age unknown)	1,437.2	494.0

* Arranged from data by Hesdorffer and Scammon.[12]

region. He stated that the order of development was first the visual area and later the temporal area, and that with the growth of each of these areas there was correlated expansion of the parietal and frontal areas, the frontal being the last to show its characteristic human development. Woollard's material for the study consisted only of the brain of an aboriginal woman and that of her newborn son.

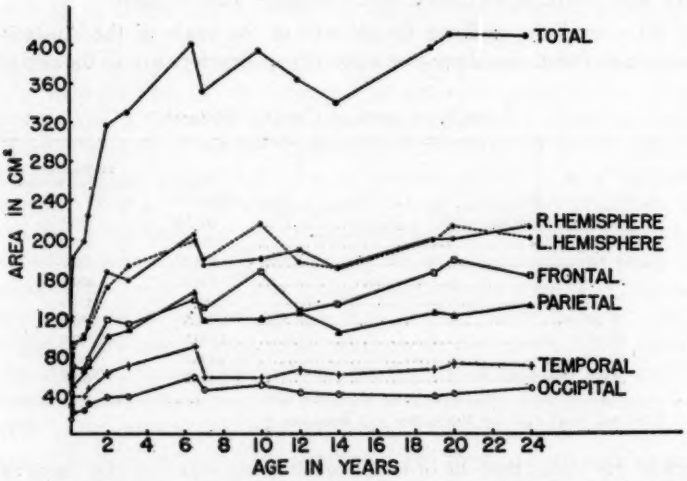
GROWTH CHANGES

When the free surface area of the two cerebral hemispheres, as well as the area of the individual hemisphere, is charted, a definite pattern of growth can be recognized, despite the irregularity of the curve due to the limited sample and the individual variations in the size of the brain (chart).

13. Woollard, H. H.: The Growth of the Brain of the Australian Aboriginal, J. Anat. **65**:224, 1931.

A very early and rapid increase in free surface area occurs within the first six years. The earliest increment appears to take place between birth and approximately 2 years of age, and during this period the area of the free cortical surface increases threefold. A second, less striking increase occurs between the ages of 2 and 6 years, and in this four year period the free surface area further increases by about 25 per cent. Between birth and 6 years of age the total free surface of the cerebrum increases about fourfold. These changes can be seen in the curves for the individual hemispheres and the curve for the entire cerebrum.

Beyond the sixth year there appears to be little change in the free surface area. No evidence could be found to indicate any difference in



Graph showing cortical surface areas of the entire cerebrum, individual hemispheres and various lobes according to age. Figures for individual lobes are those for the combined surface area of both the right and the left side.

the total surface area of the left hemisphere as compared to that of the right.

Frontal Lobe.—A comparison of the growth curves of the frontal lobes with that of the general growth curve of the cerebrum indicates differences in the pattern of expansion. In the frontal lobe there is the same rapid increase in free surface area seen in the general growth curve between birth and 2 years of age. Within this period the free surface area increases approximately threefold. The secondary period of rapid growth extends beyond the sixth year and is evident well into the tenth year of postnatal life. The general pattern of growth of the frontal lobe, as compared with that of the total visible cortex, appears to be one of less

rapid, but steadier, increase in surface area, with the active period extending from birth to the tenth year of life. During this ten year period the surface area increases to approximately four times the value at birth.

Temporal Lobe.—For the temporal lobe the period of rapid growth from birth to the second year is present in absolute, as well as relative, values, but it is less marked than for either the frontal lobe or the cerebrum as a whole. The second phase of rapid expansion occurs between the second and the sixth years, beyond which there is practically no increase in the free surface area of the lobe.

Between birth and the second year the free cortical surface increases approximately 30 per cent. From birth to the age of about 6 years the visible cortical surface undergoes expansion which approximately triples its area. As compared with the growth of the frontal lobe, that of the temporal lobe is somewhat less rapid and less extensive and is restricted to the first six years of postnatal development.

Parietal Lobe.—The general pattern of cortical expansion in the parietal lobe closely corresponds to that of the cerebrum as a whole. There is relatively rapid expansion of the cortex between birth and the second year, this being less striking in the curves of the individual hemispheres. From the second year to the age of 6 years there is a second phase of less marked expansion. Beyond the sixth year there is very little increase in visible cortical surface area.

Between birth and the second year the free cortical surface increases threefold, while between the second and the sixth year the increase is about 50 per cent. Thus, at the end of the sixth year the visible cortical surface of the parietal lobe is approximately five times that at the time of birth, the greatest increase in any lobe of the cerebrum. No definite increase is evident beyond the sixth year.

Occipital Lobe.—The general pattern of expansion in the occipital lobe differs from that in any other part of the brain in that two separate phases of rapid growth cannot be identified clearly. From birth to the sixth year the increase in surface area was practically even, with no distinct primary and secondary phases. At approximately the sixth year the free cortical surface had increased between three and four times its size at birth, and beyond this age no expansion was evident.

COMMENT

It appears from the foregoing description that the general growth of the cerebral hemisphere in postnatal life occurs between birth and the sixth year. The only exception is the frontal lobe, where the growth continues as late as the tenth postnatal year. Except in the occipital lobe, two phases of rapid growth can be identified—the first extending from

birth to the second year, and the second, somewhat less rapid and less marked, extending from the second to the sixth year. In the occipital lobe rapid growth occurs up to the sixth year, but the two phases are not clearly separated.

In terms of absolute increase, the parietal lobe appears to undergo a greater expansion than does any other lobe of the brain. There was no evidence that growth occurred earlier in any one lobe of the brain than in the others, although there was some indication that in the frontal and in the parietal lobe the process of expansion occurred at a greater rate than it did in either the temporal or the occipital lobe.

There was no evidence confirming Woollard's conclusions that the visual area developed first. There was definite indication that the frontal lobe continued to develop beyond the sixth year period of growth seen in the other lobes of the brain and in the cerebrum in general.

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PSYCHIC FUNCTION AND THE ELECTROENCEPHALOGRAM

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THE ELECTROENCEPHALOGRAM has not revealed the secret of nonorganic mental illness. In general, organic cerebral pathologic changes, including toxic changes, determine the presence of abnormality in the electroencephalogram. In the absence of such changes there is, a priori, no reason to expect abnormality of the electroencephalogram—and for the most part abnormality has not been found. Accordingly, a good deal of attention has been directed to the investigation of normal alterations in the electroencephalogram, such as changes in the alpha factor or in the amount of fast activity.

It is the purpose of this paper critically to review the literature concerning variations in the electroencephalogram with normal psychic functioning.

ALPHA ACTIVITY

1. *Alpha Activity and Perception.*—Alpha activity appears most prominently when the eyes of the subject are protected from light, and it promptly diminishes in amplitude and prevalence on exposure to light. The latency of this effect is given as 0.27 to 0.29 second when the light stimulus is of relatively high intensity, and it persists for at least 0.2 second. This latent period may vary from 0.1 to 0.9 second with decreasing intensity of the light stimulus (proportionally to its logarithm) and with decreasing duration of the flash. When alpha rhythm is not completely obliterated, it usually appears at a higher frequency, occasionally to the extent of 40 per cent (Jasper, Cruikshank and Howard [1]; Durup and Fessard [2]; Jasper and Cruikshank [3]; Cruikshank [4]; Jasper and Cruikshank [5]; Knott [6]).

1. Jasper, H. H.; Cruikshank, R. M., and Howard, H.: Action Currents from the Occipital Region of the Brain in Man as Affected by Variables of Attention and External Stimulation, Psychol. Bull. **32**:565, 1935.

2. Durup, G., and Fessard, A.: L'electrencephalogramme de l'homme: Données quantitatives sur l'arrêt provoqué par des stimuli visuels ou auditifs, Compt. rend. Soc. de biol. **122**:756, 1936.

3. Jasper, H. H., and Cruikshank, R. M.: Variations in Blocking Time of Occipital Alpha Potentials in Man as Affected by the Intensity and Duration of Light Stimulation, Psychol. Bull. **33**:770, 1936.

(Footnotes continued on next page)

The latency of this alpha-blocking effect is of the same order of magnitude as the latency of a motor response to the same stimulus. Although early observations seemed to indicate that the motor response followed the alpha-blocking effect and did not alter its latency, subsequent reports have shown that the motor response may actually precede the electroencephalographic response and decrease its latency by as much as 20 per cent, especially when the subject is urged to respond to the stimulus as promptly as possible. Also, when the subject is asked to respond to the light stimulus by counting, or when he is prepared by a continuous auditory or proprioceptive stimulus, the latency may be diminished by about 10 per cent (Durup and Fessard [2]; Jasper and Cruikshank [5]; Travis, Knott and Griffith [7]; Knott [6]).

After removal of the light stimulus, alpha activity reappears in an average of one second (± 0.5 second). However, when the light continues for more than three seconds, alpha may begin to recover and may adapt completely. The blocking effect recurs when the light is removed and again presented. Moreover, alpha activity has been reported to fluctuate with visual after-images in the same fashion as it does with light, though less markedly. A later paper by Travis and Hall confirmed the depression of alpha activity in the presence of visual after-images, but only when active attention is given to them (Jasper, Cruikshank and Howard [1]; Jasper and Cruikshank [5]; Travis and Knott [8]; Travis and Hall [9]).

It is standard clinical practice to record the electroencephalogram with the subject in a not too brightly lighted room with his eyes closed. In these circumstances a maximum alpha content is obtained. Opening the eyes depresses the alpha amplitude and the alpha factor and increases its frequency, as does the presentation of a light stimulus in a dark

4. Cruikshank, R. M.: Human Occipital Brain Potentials as Affected by Intensity-Duration Variables of Visual Stimulation, J. Exper. Psychol. **21**:625, 1937.

5. Jasper, H., and Cruikshank, R. M.: Electroencephalography: II. Visual Stimulation and the After-Image as Affecting the Occipital Alpha Rhythm, J. Gen. Psychol. **17**:29, 1937.

6. Knott, J. R.: Some Effects of "Mental Set" on the Electrophysiological Processes of the Human Cerebral Cortex, J. Exper. Psychol. **24**:384, 1939.

7. Travis, L. E.; Knott, J. R., and Griffith, P. E.: Effect of Response on the Latency and Frequency of the Berger Rhythm, J. Gen. Psychol. **16**:391, 1937.

8. Travis, L. E., and Knott, J. R.: Brain Potential Studies of Perseveration: I. Perseveration Time to Light, J. Psychol. **3**:97, 1937.

9. Travis, L. E., and Hall, M. E.: Effect of Visual After-Sensations upon Brain Potential Patterning Under Different Degrees of Attention, J. Exper. Psychol. **22**:472, 1938.

room. According to Redlich, Callahan and Mendelson,[10] the effect is pronounced in about 1 of 2 subjects and undiscernible in about 1 of 10. The latency varies up to one second. Alpha activity returns when the eyes are closed, though, as previously noted, it may recur even with the eyes open in a lighted room after a number of seconds. Even in a completely dark room, opening the eyes depresses the alpha activity, but here it returns more quickly than in the light. Moreover, opening one eye is as effective as opening both eyes, even though the eye opened be the blind eye in a unilaterally blind person. However, opening the eyes fails to depress alpha activity in totally blind persons. It would seem, then, that opening the eyes in a dark room depresses alpha activity by virtue of the fact that opening the eyes is usually associated with admission of light to the eye, that is, by virtue of a conditioned reflex.

Beritoff and Vorobjev,[11] considering the situation with the eyes open the standard one, investigated the response to shading or closing the eyes. Shading, they found, evoked an increase in alpha activity in one to three seconds, and closing the eyes evoked the same response within half a second. If the eyes remained shaded or closed, the alpha activity again became less prominent within a few seconds, but facilitation could once more be evoked by opening and then closing the eyes. However, this facilitating effect on alpha activity of closing the eyes subsides after a number of repetitions, and a point arrives when opening the eyes or exposing them to light actually facilitates the appearance of alpha activity. These observations suggest not only that the closed-open status of the eyes obtains its effectiveness in affecting alpha activity by a conditioning mechanism but that even the effect of light itself may be determined by its signal value rather than by a direct stimulus-response mechanism (Beritoff and Vorobjev[11]).

In this connection, it is interesting to note that both Cruikshank and Jasper have reported a response to light stimulation independent of the depression of alpha activity. This they called the evoked potential, or "on effect." Its most constant feature is a slow positive swing, which is less susceptible to conditioning and visual attention than the depression of alpha rhythm. The magnitude of the evoked potential varies directly with the logarithm of the intensity of the light stimulus,

10. Redlich, F. C.; Callahan, A., and Mendelson, R. H.: Electroencephalographic Changes After Eye Opening and Visual Stimulation, Yale J. Biol. & Med. **18**:367, 1946.

11. Beritoff, J., and Vorobjev, A.: On the Origin of the Facilitating Action on Alpha Waves in Man, Caused by Closing the Eyes, Tr. J. Beritashvili Institute **5**:369, 1943.

and its latency varies from 60 to 150 milliseconds, with diminution in the brightness of the light source over a range of 10^4 (Jasper [12] 1936; Cruikshank [4]).

Alpha activity is depressed by sound stimuli less constantly than by light stimuli. Different observers have reported 10 to 50 per cent of subjects responsive to sound stimulation. The latency of this effect is given as 0.33 to 0.5 second. When the subject is asked to discriminate between two tones and to execute an appropriate motor response, depression of alpha activity follows the tone stimulus twice as often as in the control situation. The motor response may precede the depression of alpha activity, especially when speed is demanded of the subject. Moreover, the latency of the alpha depression may be diminished as much as 16 per cent when a motor response is required of the subject. When the sound continues, alpha activity recurs more promptly than in the presence of an intermittent sound or of a continuing visual stimulus (Jasper, Cruikshank and Howard [1]; Durup and Fessard [2]; Bagchi [13]; Travis, Knott and Griffith [7]; Travis and Egan [14]; Bakes [15]).

When sound and light stimuli are presented within a short time of each other, the sound stimulus becomes a potent depressor of alpha activity by means of a conditioning process which fulfils the classic pavlovian criteria. On the other hand, when the sound stimulus is combined with closing or shading the eyes, it becomes the conditioned stimulus for an increase in alpha activity. Jasper and Cruikshank suggested that a sound stimulus depresses alpha activity only when the sound is a signal or produces a startle effect (Davis and Davis [16]; Jasper and Cruikshank [5]; Travis and Egan [14]; Jasper and Shagass [17]; Knott and Henry [18]; Beritoff and Vorobjev [11]).

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12. Jasper, H. H.: Cortical Excitatory State and Synchronism in the Control of Bioelectric Autonomous Rhythms, in Cold Spring Harbor Symposia on Quantitative Biology, Cold Spring Harbor, L. I., New York, The Biological Laboratory, 1936, vol. 4, p. 320.

13. Bagchi, B. K.: The Adaptation and Variability of Responses of the Human Brain Rhythm, J. Psychol. **3**:463, 1937.

14. Travis, L. E., and Egan, J. P.: Increase in Frequency of the Alpha Rhythm by Verbal Stimulation, J. Exper. Psychol. **23**:384, 1938.

15. Bakes, F. P.: Effect of Response to Auditory Stimulation on the Latent Time of Blocking of the Berger Rhythm, J. Exper. Psychol. **24**:406, 1939.

16. Davis, H., and Davis, P. A.: Action Potentials of the Brain in Normal Persons and in Normal States of Cerebral Activity, Arch. Neurol. & Psychiat. **36**:1214 (Dec.) 1936.

17. Jasper, H., and Shagass, C.: Conditioning the Occipital Alpha Rhythm in Man, J. Exper. Psychol. **20**:373, 1941.

18. Knott, J. R., and Henry, C. E.: The Conditioning of the Blocking of the Alpha Rhythm of the Human Electroencephalogram, J. Exper. Psychol. **28**:134, 1941.

Less information is available concerning the effects of tactile stimuli. Jasper and Andrews [19] reported that auditory or tactile stimuli may block precentral beta activity without affecting occipital alpha activity. Travis and Barber [20] found tactile stimuli effective in depressing alpha activity in 20 to 40 per cent of trials, with a latency of about 0.5 second, the effect persisting about one second after removal of the stimulus. Beritoff and Vorobjev [11] observed that simulation of the recumbent position by pressure on the back increases alpha activity, and they stated the belief that the effect is a conditioned one, operating by virtue of the constant association between recumbency and repose. Jasper and Cruikshank stated that tactile and painful stimuli are effective in depressing alpha activity only when they are signals or evoke a startle reaction (Jasper and Cruikshank [5]; Jasper and Andrews [19]; Travis and Barber [20]; Beritoff and Vorobjev [11]).

2. *Alpha Activity and Cerebration.*—Early observers noted that not only the perception of stimuli but mental activity as well provoked depression of alpha activity. As already mentioned, there are hints that perhaps the depression of alpha rhythm following perception of a stimulus may be a consequence of the psychic significance of the perception rather than an innate, unconditioned reflex response. Much work has been devoted to the elucidation of the precise nature of the mental activity or attitude which is associated with depression of alpha activity.

The performance of a simple hand movement is not associated with electroencephalographic change, so that the mental acts of intention and volition cannot be considered depressors of alpha activity (Adrian and Matthews [21]; Jasper, Cruikshank and Howard [1]; Jasper and Cruikshank [5]).

The elaboration of the stimulus situation to the end that the object perceived becomes less indifferent or the subject more active in the perception results in a greater depression of alpha activity than that noted in the uncomplicated experiments summarized in the previous section. Bagchi [13] observed that the presentation of a series of words, rather than a series of pure tones, resulted in the prolongation of the adaptation time (time required for recovery of alpha activity following its initial depression). The substitution of a pattern for a lighted uniform visual field, in the experiments of Adrian and Matthews,[21]

19. Jasper, H. H., and Andrews, H. L.: Electroencephalography: III. Normal Differentiation of Occipital and Precentral Regions in Man, Arch. Neurol. & Psychiat. **39**:96 (Jan.) 1938.

20. Travis, L. E., and Barber, V.: The Effect of Tactile Stimulation upon the Berger Rhythm, J. Exper. Psychol. **22**:269, 1938.

21. Adrian, E. D., and Matthews, B. H. C.: The Berger Rhythm: Potential Changes from the Occipital Lobes in Man, Brain **57**:355, 1934.

evoked a distinct depression of alpha activity. Even an attempt to see detail in the uniform field had the same effect. Concurring, Jasper and Cruikshank [5] reported that the attempt to see in a dark room resulted in depression of alpha activity, and Toman [22] reported that perception of a dimly lighted pattern did the same. In experiments performed by Travis and Knott,[23] the recovery of alpha activity following depression induced by presentation of flash cards required a longer period when the cards bore words or nonsense words than when the cards were blank. Reading is an effective depressor of alpha activity, oral reading more so than silent (Knott [24]; Williams [25]; Redlich, Callahan and Mendelson [10]).

A startle response, no matter how provoked, is constantly associated with pronounced depression of alpha activity. (Adrian and Matthews [21]; Davis and Davis [16]; Bagchi [13]; Delay [26]).

More abstract forms of mental activity, such as imagery and calculation, are less susceptible to experimental control, and so the results are less consistent. Thus, Adrian and Matthews [21] failed to observe depression of alpha activity during visual imagery; Travis [27] found lower alpha voltage during preoccupation with visual images than during "mental blankness" or "abstract thinking," and Redlich, Callahan and Mendelson [10] noted diminution of alpha amplitude during visual imagery in 9 of 42 subjects. It is more generally accepted that mental arithmetic or the solution of problems impairs alpha activity, and that the more difficult the problem the greater the effect (Adrian and Matthews [21]; Davis and Davis [16]; Jasper and Cruikshank [5]; Travis [27]; Martinson [28]). Toman,[22] on the other hand, discerned no significant difference between the mean per cent time alpha values for 64 subjects at rest and those obtained during continuous calculation of an arithmetical progression. But even in this experiment, two thirds of his subjects showed decrease in per cent time alpha during mental effort, and more than one half showed a decrease in alpha voltage.

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22. Toman, J. E. D.: The Electroencephalogram During Mental Effort, Federation Proc. **2**:49, 1943.

23. Travis, L. E., and Knott, J. R.: Brain Potential Studies of Perseveration: Perseveration Time to Visually Presented Words, J. Exper. Psychol. **21**:353, 1937.

24. Knott, J. R.: Brain Potentials During Silent and Oral Reading, J. Gen. Psychol. **18**:57, 1938.

25. Williams, A. C.: Some Psychological Correlates of the Electroencephalogram, Arch. Psychol. **34**:240, 1939.

26. Delay, J.: Les ondes cérébrales et la psychologie, Presses Universitaires de France, Paris, 1942.

27. Travis, L. E.: Brain Potentials and the Temporal Course of Consciousness, J. Exper. Psychol. **21**:302, 1937.

28. Martinson, B. M.: A Study of Brain Potentials During Mental Blocking, J. Exper. Psychol. **24**:143, 1939.

Since attitudes are even more difficult to establish or ascertain, their study gives rise to a greater indefiniteness and disagreement among investigators. Attention, though variously and vaguely defined, is said by many to give rise to a depression of alpha activity (Adrian and Matthews [21]; Jasper, Cruikshank and Howard [1]; Jasper and Cruikshank [5]; Delay [26]). Williams,[25] however, protested that a state of attentiveness, alone, is not sufficient to produce inhibition of alpha activity; attention to a specific stimulus is required. Martinson [28] could find no correlation between alpha activity and mental blocking, a sudden, involuntary cessation of mental work occurring at intervals after prolonged application. Anxiety, apprehension and "nervousness" were recorded as situations inhibiting the appearance of alpha activity (Davis and Davis [16]; Jasper and Cruikshank [5]). Oberman [29] demonstrated statistically significant depression of alpha activity on mild emotional stimulation of subjects in a laboratory situation.

Alpha activity may suddenly increase in amplitude and regularity for a few seconds; this phenomenon is called facilitation. Bagchi [13] observed facilitation immediately after the removal of auditory stimuli, and Toman,[22] after the removal of visual stimuli. Beritoff and Vorobjev's [11] statement that closure of the eyes is promptly followed by increase in alpha voltage lasting a few seconds probably refers to the facilitation effect. Williams [30] and Strauss [31] called attention to the fact that hyperventilation frequently provokes a sudden, prompt increase in alpha voltage and per cent time, long before any significant alteration in the p_H carbon dioxide concentration of the blood can develop. In a careful study of facilitation, Williams learned that it was evoked by situations calling forth a sudden mobilization of the subject's reactive apparatus—a state of attentiveness or readiness or increased awareness. It occurred, for example, after the ready signal before a projected task, while the subject was answering simple questions, after a period of being given instructions and even immediately after the completion of a given task. After a given stimulus situation has been repeated several times, facilitation fails to appear, presumably because by virtue of the repetition the significance of the situation has been affected. This observation seems related to the report of Beritoff and Vorobjev [11] that after several repetitions closure or shading of the eyes fails to facilitate alpha activity; at this point, opening or exposure of the eye to light develops an alpha-facilitating effect.

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29. Oberman, C. E.: The Effect on the Berger Rhythm of Mild Affective States, J. Abnorm. & Social Psychol. **34**:84, 1939.

30. Williams, A. C.: Facilitation of the Alpha Rhythm of the Electroencephalogram, J. Exper. Psychol. **26**:413, 1940; footnote 25.

31. Strauss, H.: Clinical and Electroencephalographic Studies: The Electroencephalogram in Psychoneurotics, J. Nerv. & Ment. Dis. **101**:19, 1945.

Additional light is thrown on the situation by Jasper's [12] observation that if the intensity of psychic activity can be considered as increasing continuously from very deep sleep to intense excitement, then alpha activity is most prominent at about the middle of the range, a point of moderate relaxation. At this point, either further excitement or further lapse into drowsiness results in a diminution of alpha activity.

It should be noted parenthetically that most of the observations aforementioned were based on records derived from occipital leads. The effects are qualitatively the same in areas presenting less intense spontaneous alpha rhythm, but are somewhat attenuated. Most authors have indicated, also, that the direction of the alterations is independent of the basal per cent time alpha of the subject. It seems to be a general rule, too, that when alpha activity is depressed by any stimulus situation (not by sleep) its frequency is increased (Jasper [12]; Jasper and Cruikshank [3]; Cruikshank [4]; Travis and Egan [14]; Martinson [28]; Redlich, Callahan and Mendelson [10]).

In 1948, a description of "kappa waves" appeared. These (kappa, or Kennedy, waves) were waves of alpha frequency recorded by bipolar electrodes just behind the external canthi of the eyes which appeared to become prominent during discrimination, mental arithmetic and problem-solving activities. They occurred in less than half the population. Although this observation has not been confirmed in the literature, it is easily reproducible. However, assigning a new name to these waves tends to obscure the issue somewhat. We believe that the observation can be more simply stated in the following form: During active cerebration, alpha activity in the temporal region is reenforced. It seems to us that only confusion is engendered by calling 8 to 12 per second activity in the occipital region alpha activity and that in the temporal region kappa waves. It is not clear at this point whether this electrical activity is derived directly from whatever physiologic process is responsible for the mental activity or whether it merely represents a release of the temporal lobe from domination by other pacemakers (Kennedy, Gottsdanker, Armington and Gray [32]).

3. *Inferences and Comment.*—From their experiences, Adrian and Matthews [21] concluded that alpha activity represents a spontaneous beat of the visual cortex, which is broken up by exposing the visual cortex to nonuniform excitation. Travis [27] inferred that the "factors effective in disturbing the alpha rhythm are those which focus consciousness."

> The large brain potentials . . . represent a generalized psychic activity, while a break up of this collective action into more rapid and irregular oscillations of much smaller amplitude represents a relatively high degree of specificity in psychic activity.

32. Kennedy, J. L.; Gottsdanker, R. M.; Armington, J. C., and Gray, F. E.: A New Electroencephalogram Associated with Thinking, Science **108**:527, 1948.

Williams [25] preferred a dualistic hypothesis. Alpha is determined (*a*) by local synchronization and (*b*) by the action of central (subcortical) pacemakers. Directed mental effort depresses alpha activity by interfering with local synchronization, and sleep depresses alpha activity by its effect on the central pacemakers. Strauss [31] suggested that high per cent time alpha indicates relaxation and freedom from emotional tension. Redlich, Callahan and Mendelson [10] ascribe inhibition of alpha activity to a shift from one type of cerebral function at rest and relaxation to another type induced by opening the eyes and visual stimulation, namely, "activation for the perception of light and form."

The data we have reviewed strongly support Jasper and Cruikshank's suggestion that pain, touch and sound stimuli depress alpha activity by virtue of their signal value. Moreover, it seems that even the usual depressing effect of visual stimulation on alpha rhythm may be reversed by changing the significance of the stimulus. Actually, the most constant depressors of alpha activity are the startle phenomenon, on the one hand, and sleep, on the other. Alpha activity is facilitated by an alert, expectant attitude. Obviously, then, alpha activity does not appear unless the brain is fully awake and ready to function. On the other hand, alpha activity is depressed during active cerebration. Apparently, it is the state of readiness, the situation in which the brain is operating without a "load," like an automobile motor idling, that is the specific condition for prevalence of alpha activity. Dissipation of the alpha activity follows the call for active cerebration or the surrender of consciousness, as in sleep. The call for cerebration is a function of the complexity of the environment and the subject's interest in it. Thus, pattern vision and a startle situation are both effective depressors of alpha activity.

If one considers cerebration to be the organization of a number of discrete data into a meaningful psychic pattern, then one would expect, with perception at least, that the greater the number of discrete data in the stimulus situation, the greater the depression of alpha activity. Thus, visual stimuli include a larger number of data than auditory at any given instant, and auditory stimuli, a larger number than tactile. Accordingly, visual stimuli are most effective in depression of alpha activity; auditory stimuli are less so and tactile stimuli least. However, the effectiveness of any modality of stimulation in depressing alpha activity may be increased or decreased by increasing or decreasing the number of component data included and increasing or decreasing the affective significance of the stimuli.

INFLUENCE OF EMOTION ON THE ELECTROENCEPHALOGRAM

The appearance of apprehension, "tension," "nervousness," "autonomic tension," emotional stress or excitement in the course of the electroencephalographic examination sharply depresses the amount of

alpha activity yielded (Davis and Davis [16]; Jasper and Cruikshank [5]; Hughes, Strecker and Appel [33]). The alpha potential is usually replaced by low voltage, random frequency activity or by fairly distinct fast activity (18 to 20 cycles per second).

When the subject was confronted with mild affective states in the laboratory, such as being forced to tell a lie, asked for free association to stimulus words with pleasant or unpleasant connotation or embarrassed with personal questions, depression of alpha activity resulted (Oberman [29]). The same type of experiment was performed by Hoagland, Cameron and Rubin,[34] who reported an increase in pulse rate and "delta index" (a measure of per cent time delta) when the subject was embarrassed by questioning. However, the records presented in their paper show a low voltage delta activity synchronous with the electrocardiogram following the presentation of the stimulus. Much of the delta activity seems artifactual. Moreover, their results could not be reproduced by Thiesen,[35] who used disturbing stimuli, such as moving pictures of a rat being killed and eviscerated, a live rat held above the subject's head and electric shocks to the hand. He found no elevation of the delta index—in fact, no change which could be considered a clinical abnormality. The only electroencephalographic change which followed the stimuli was flattening of the record, and frequently a decrease in the per cent time beta from frontal and motor electrodes.

"Irregular, partially synchronous giant waves and plateaus with frequent cusps" were reported by Grinker and Serota [36] to follow the presentation of embarrassing statements when records were derived from pharyngeal or occipital electrodes and ear electrodes. Hoagland, Cameron, Rubin and Tegelberg [37] reported similar results.

Nevertheless, the provocation of delta activity by anxiety-laden situations is not generally accepted today. Prominent fast activity is frequently observed in anxious psychoneurotic patients.

Anxiety may perhaps be thought of as consisting of several elements: (*a*) fear of impending danger (which may or may not have a specific

33. Hughes, J.; Strecker, E. A., and Appel, K. E.: Some Clinical and Physiological Aspects of the Brain Potentials, Am. J. Psychiat. **94**:1179, 1938.

34. Hoagland, H.; Cameron, D. E., and Rubin, M. A.: Emotion in Man as Tested by the Delta Index of the Electroencephalogram: I., J. Gen. Psychol. **19**: 227, 1938.

35. Thiesen, J. W.: Effects of Certain Forms of Emotion on the Normal Electroencephalogram, Arch. Psychol. **40**:285, 1943.

36. Grinker, R. R., and Serota, H.: Studies on Corticohypothalamic Relations in the Cat and Man, J. Neurophysiol. **1**:573, 1938.

37. Hoagland, H.; Cameron, D. E.; Rubin, M. A., and Tegelberg, J. J.: Emotion in Man as Tested by the Delta Index of the Electroencephalogram: II. Simultaneous Records from Cortex and from a Region near the Hypothalamus, J. Gen. Psychol. **19**:247, 1938.

object, either real or projected, and either present in the perceivable environment or elsewhere); (*b*) overactivity of the sympathetic nervous system; (*c*) subjective perception of sympathetic overactivity, e. g., palpitation, tremulousness or dizziness, and (*d*) drive to protective, aggressive activity. There is no evidence that *a*, *b*, or *c* has any effect on alpha activity, while *d* will probably have such an effect. This drive to protective aggressive activity may take either of two forms: (1) a mobilization of resources, mental and physical, in readiness for confrontation by the dangerous situation, or (2) mental or physical overactivity (or both) relatively undirected during the period of anticipation, or sharply directed, in the presence of the dangerous situation. Such mental overactivity consists of analytic cerebration, in my opinion, the specific dissipator of alpha activity. The anticipatory mobilization of the first form, on the other hand, I have described as the specific facilitator of alpha activity. Of course, the anxious patient may be concerned about the recording situation itself or may have another source of anxiety. Activity of type 1 with respect to either an immediate or a remote source of anxiety will be associated with a high per cent time alpha, while activity of type 2 will depress the per cent time alpha.

CORRELATION BETWEEN INTELLIGENCE AND THE ELECTROENCEPHALOGRAM

There is no relation between any feature of the electroencephalogram and the intelligence of nondefective persons. Shagass [38] found no correlation between occipital alpha frequency and the intelligence score on a group test of mental ability in a series of 1,100 Canadian air crew candidates. Among 42 subjects 12 years of age, likewise, Knott, Friedman and Bardsley [39] found no relation between alpha frequency and intelligence quotient. However, the same authors observed a definite association between these two factors in a group of 48 subjects aged 8 years, with a correlation coefficient of 0.50. Abnormal records do occur among mentally defective subjects.

INFLUENCE OF THE STATE OF CONSCIOUSNESS ON THE ELECTROENCEPHALOGRAM

Alteration of the state of consciousness due to organic functional or structural cerebral changes is constantly associated with slowing of the electroencephalogram. In general, the more profound the depression of

38. Shagass, C.: An Attempt to Correlate the Occipital Alpha Frequency of the Electroencephalogram with Performance on a Mental Ability Test, J. Exper. Psychol. **36**:88, 1946.

39. Knott, J. R.; Friedman, H., and Bardsley, R.: Some Electroencephalographic Correlates of Intelligence in Eight-Year- and Twelve-Year-Old Children, J. Exper. Psychol. **30**:380, 1942.

consciousness, the greater the slowing (Engel and Romano [40]). Further, there is a rise in amplitude as well, until a given point when, possibly because of failure of primitive vital functions, the amplitude begins to decrease and ultimately becomes flat and remains so until death.

The slowing is evident even in the presence of mere clouding of consciousness. Patients with clouding of consciousness or facetiousness due to organic cerebral disease show a greater mean delta factor than patients with organic cerebral disease but without clouding of consciousness or facetiousness (Strauss [41]). The mean delta factor is the same among patients with clouding of consciousness and facetious patients, but among the latter the delta factor appears maximally in both frontal regions.

In addition to that of Berger, the names of Loomis, Pauline and Hallowell Davis, Harvey, Hobart and Blake are associated with the classic descriptions of sleep, and their findings still stand. Typically, in the subject with good alpha activity, the first alteration is a flattening of the record. If he is questioned at this point, the subject will say that he is drowsy but not asleep. As drowiness deepens, fairly regular, sinusoidal, 4 to 6 per second activity appears in longer and longer runs at low to moderate voltages. At this point many subjects will say that they have been asleep, though others may acknowledge only drowsiness. As sleep deepens, runs, referred to in the literature as spindles, of 12 to 15 cycles per second and moderate voltage, appear at times alone, and at times superimposed on the slow activity. With still further profundity of sleep, the fast activity disappears, and slow activity becomes slower and of higher voltage. Finally, in deepest sleep, the record consists of high voltage fluctuations at ½ to 2 cycles per second. This sequence of electrical activity is reversed in the waking process. However, since the latter is usually more abrupt than the former, all the stages may not be permitted to appear. The fast activity, for example, is usually less conspicious during the ascending than during the descending phase of sleep. (Blake [42]; Blake and Gerard [43]; Davis, Davis, Loomis and Harvey [44];

40. Engel, G. L., and Romano, J.: Delirium: II. Reversibility of the Electroencephalogram with Experimental Procedures, Arch. Neurol. & Psychiat. **51**:378 (April) 1944.

41. Strauss, H.: Clinical and Electroencephalographic Studies, Am. J. Psychiat. **101**:42, 1944.

42. Blake, H.: Brain Potentials and Depth of Sleep, Am. J. Physiol. **119**:273, 1937.

43. Blake, H., and Gerard, R. W.: Brain Potentials During Sleep, Am. J. Physiol. **119**:692, 1937.

44. Davis, H.; Davis, P. A.; Loomis, A. L., and Harvey, E. N.: Changes in Human Brain Potentials During the Onset of Sleep, Science **86**:448, 1937.

Blake, Gerard and Kleitman [45]; Davis, Davis, Loomis, Harvey and Hobart.[46])

All this activity is in general symmetric. The location of the mechanism governing electrocortical changes during sleep has thus far eluded detection. However, amplitude gradients and phase reversals indicate the sites of the most direct projections from the sources to the cortex. Most of this work has been done by Liberson [47] and Brazier.[48] Foci of origin of slow and fast sleep activity have been found at the vertex and at the precentral and frontal regions symmetrically.

Dreams are not recognizable by specific changes in the electroencephalogram. They are thought to occur during the B stage of sleep, that is, when the record has become flat, after the dissappearance of alpha activity and before the appearance of slow waves or spindles (Loomis, Harvey and Hobart [49]).

During the hypnotic trance, the electroencephalogram is not changed from the usual waking record (Dynes [50]; Loomis, Harvey and Hobart [51]; Lundholm and Löwenbach [52]).

Lemere [53] and Lundholm and Löwenbach [52] described depression of alpha activity when the eyes are open despite hypnotically induced blindness, and prominent alpha activity with the eyes closed despite hypnotically induced visual hallucinations. The latter authors stated that alpha activity responds to light in the usual fashion despite hysterical blindness. Loomis, Harvey and Hobart,[51] however, described the appearance of "alpha trains" during hypnotically suggested return of vision. These discrepancies can probably be resolved by analyzing the actual situation in terms of readiness and the call to cerebration, as previously described. One may think of the hypnotic situation as a

45. Blake, H.; Gerard, R. W., and Kleitman, N.: Factors Influencing Brain Potentials During Sleep, J. Neurophysiol. **2**:48, 1939.

46. Davis, H.; Davis, P. A.; Loomis, A. L.; Harvey, E. N., and Hobart, G.: Human Brain Potentials During the Onset of Sleep, J. Neurophysiol. **1**:24, 1938.

47. Liberson, W. T.: Problem of Sleep and Mental Disease, Digest Neurol. & Psychiat., Inst. of Living **12**:93, 1944; Functional Electroencephalography in Mental Disorders, Dis. Nerv. System **5**:1, 1945.

48. Brazier, M. A. B.: The Electrical Fields at the Surface of the Head During Sleep, Electroencephalog. & Clin. Neurophysiol. **1**:195 (May) 1949.

49. Loomis, A. L.; Harvey, E. N., and Hobart, G. A.: Brain Potentials During Sleep, J. Exper. Psychol. **21**:127, 1937.

50. Dynes, J. B.: Objective Method for Distinguishing Sleep from the Hypnotic Trance, Arch. Neurol. & Psychiat. **57**:84 (Jan.) 1947.

51. Loomis, A. L.; Harvey, E. N., and Hobart, G.: Brain Potentials During Hypnosis, Science **83**:239, 1936.

52. Lundholm, H., and Löwenbach, H.: Hypnosis and the Alpha Activity of the Electroencephalogram, Character and Personality **11**:145, 1942.

53. Lemere, F.: The Signifinance of Individual Differences in the Berger Rhythm, Brain **59**:366, 1936.

form of motivation which per se has no effect on the electroencephalogram. The actual state of readiness or of cerebration is the effective factor in determining the prevalence of alpha activity no matter what the motivation.

THE ELECTROENCEPHALOGRAM AND PERSONALITY

On the basis of his impression that patients with manic-depressive psychosis show a "good alpha rhythm" and schizophrenic patients a "poor alpha rhythm," Lemere [53] suggested that alpha rhythm might be a measure of "affective strength." Extroversion was found by Gottlober [54] to be associated with a per cent time alpha of over 50. Henry and Knott,[55] however, using the same test for evaluation of extroversion (Nebraska personality inventory test), were unable to confirm Gottlober's findings.

Seventy patients analyzed at the Chicago Institute for Psychoanalysis were separated into two groups, those with a high per cent time alpha and those with a low per cent time alpha (Saul, Davis and Davis [56]; Davis and Davis [57]; Davis [58]). The former group was composed of patients with a passive, dependent, receptive attitude, characterized as patient workers and stable citizens. The subjects in the latter group exhibited a consistent, indulged, well developed drive to activity. Essentially the same conclusions were reached in studies of patients with peptic ulcer (Rubin and Bowman [59]), with bronchial asthma (Rubin and Moses [60]) and with duodenal ulcer (Moses [61]).

The relation of the alpha factor to personality is perhaps best understood by referring to the recording situation itself. The subject who,

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54. Gottlober, A. B.: The Relationship Between Brain Potentials and Personality, J. Exper. Psychol. **22**:67, 1938.

55. Henry, C. E., and Knott, J. R.: A Note on the Relationship Between "Personality" and the Alpha Rhythm of the Electroencephalogram, J. Exper. Psychol. **28**:362, 1941.

56. Saul, L. J.; Davis, H., and Davis, P. A.: Correlations Between Electroencephalograms and the Psychological Organization of the Individual, Tr. Am. Neurol. A. **63**:167, 1937; Psychological Correlations with the Electroencephalogram, presented at the Third Annual Meeting of the American Electroencephalographic Society, Atlantic City, N. J., June 11-13, 1949.

57. Davis, H., and Davis, P. A.: The Electrical Activity of the Brain: Its Relation to Physiological States and to States of Impaired Consciousness, A. Research Nerv. & Ment. Dis., Proc. (1937) **19**:50, 1938.

58. Davis, P. A.: Development of Electroencephalography: Retrospect and Outlook, Am. J. Orthopsychiat. **10**:710, 1940.

59. Rubin, S., and Bowman, K. M.; Electroencephalographic and Personality Correlates in Peptic Ulcer, Psychosom. Med. **4**:309, 1942.

60. Rubin, S., and Moses, L.: Electroencephalographic Studies in Asthma with Some Personality Correlates, Psychosom. Med. **6**:31, 1944.

61. Moses, L.: Psychodynamic and Electroencephalographic Factors in Duodenal Ulcer, Psychosom. Med. **8**:405, 1946.

when told to sit or lie comfortably without actively participating in the procedure, thereafter surrenders himself to "passive" thinking, that is, free association, daydreaming or phantasying, will very likely yield a record with a high per cent time alpha. On the other hand, the subject who in such circumstances refuses to assume a passive attitude, preferring to think actively ("cerebrate"), even though physically at rest (or perhaps even because physically at rest), will show a low alpha factor (Travis [27]). This interpretation is supported by the observations of Knott, Henry and Hadley,[62] as well as Henry,[63] on groups of subjects who were heterogeneous with respect to per cent time alpha in the waking state. The sleep records of all the subjects were almost identical, and the per cent time alpha immediately on awakening was fairly uniform. Such heterogeneity was reduced also by requiring taxing mental tasks of the subjects. These authors inferred that the great differences observed in the waking records with respect to per cent time alpha might be ascribed to differences in the relation of the person to his environment.

Among 200 schoolboys examined by Gallagher, Gibbs and Gibbs,[64] there was a tendency for "poor" personalities to be associated with dominantly slow electroencephalograms and for "good" personalities to be associated with dominantly fast electroencephalograms.

Classifying schizophrenic patients according to type of imagery, Rubin and Cohen [65] observed a higher per cent time alpha among patients with kinesthetic imagery than among patients with tactual-thermal imagery. The heterogeneity in each group with respect to per cent time alpha was much less than the heterogeneity in a group of normal subjects, whose mean per cent time alpha fell between those of the two schizophrenic groups. Another attempt to relate electroencephalographic patterns to imagery was made by Golla, Hutton and Walter.[66] They distinguish three groups of normal subjects, thus: (1) those with no alpha rhythm with eyes closed or with eyes open; (2) those with

62. Knott, J. R.; Henry, C. E., and Hadley, J. M.: Brain Potentials During Sleep: A Comparative Study of the Dominant and Non-Dominant Alpha Groups, J. Exper. Psychol. **24**:157, 1939.

63. Henry, C. E.: Electroencephalographic Individual Differences and Their Constancy: I. During Sleep, J. Exper. Psychol. **29**:117, 1941; II. During Waking, ibid. **29**:236, 1941.

64. Gallagher, J. R.; Gibbs, E. L., and Gibbs, F. A.: Relation Between the Electrical Activity of the Cortex and the Personality in Adolescent Boys, Psychosom. Med. **4**:134, 1942.

65. Rubin, M. A., and Cohen, L. H.: A Variability Study of the Normal and Schizophrenic Occipital Alpha Rhythm: II. The Electroencephalogram and Imagery Type, J. Ment. Sc. **85**:779, 1939.

66. Golla, F.; Hutton, E. L., and Walter, W. G.: The Objective Study of Mental Imagery, J. Ment. Sc. **89**:216, 1943.

alpha activity when the eyes were closed, but whose alpha activity disappeared when the eyes were opened, and (3) those with good alpha activity whether the eyes were open or closed. The subjects in group 1 seemed disposed primarily to visual imagery; the subjects in group 3 seemed disposed primarily to audiokinetic imagery, whereas the subjects of group 2 seemed to employ a combination of the two types of imagery. It seems to us that the three groups probably represent variations in the strength of the conditional association between opening the eyes and the call to cerebration. This association is perhaps relatable to type of imagery.

The absence of any relation between per cent time alpha and "mental fatigue" was asserted by Barnes and Brieger.[67] They found no significant difference between the per cent time alpha of 27 medical students at 8 a. m. and at 5 p. m. of the academic day. The phenomenon of mental blocking, that is, the sudden brief inability to continue after a long period of persistent, taxing mental work, was demonstrated by Martinson [28] to be unrelated to per cent time alpha.

SUMMARY

It is fairly clear that there is no departure from the range of normal frequencies as a result of any variation within the normal range of psychic function as long as the subject remains awake. The prevalence of alpha activity is increased by readiness for constructive cerebration and is dissipated by constructive cerebration itself. Affective states per se are without influence on the electroencephalogram, but whatever alterations in the state of intellectual function are evoked by the affective states are reflected in changes in the prevalence of alpha rhythm. Similarly, variations from subject to subject in the electroencephalographic pattern reflect a personality difference only to the extent that habits of constructive, intellectual function vary.

50 East Seventy-Eighth Street (21).

67. Barnes, T. C., and Brieger, H.: Electroencephalographic Studies of Mental Fatigue, J. Psychol. **22**:181, 1946.

MYELOMALACIA SECONDARY TO DISSECTING ANEURYSM OF THE AORTA

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PHILADELPHIA

INVOLVEMENT of the nervous system has been reported in numerous cases of dissecting aneurysm of the aorta.[1] The neural complications have been produced by an ischemic necrosis. The peripheral nerves, the spinal cord and even the brain have been affected.[1b] Softening of the spinal cord has occurred when the aneurysmal dissection severed the intercostal or lumbar arteries from the aorta, when a thrombus blocked these vessels directly or otherwise isolated them from the main circulation or when the dissection extended into these branch arteries and choked off their lumens.

Most of the reports on the neurologic occurrences with dissecting aneurysms of the aorta either have been entirely clinical or have been accompanied with an inadequate examination of the nervous system at necropsy. In only 3 cases [2] have we been able to find a description of the changes within the spinal cord. Such studies would seem to afford an opportunity to estimate the functional capacity of the arterial circulation of the spinal cord in man. Because of the rarity of this complication and because of the chance to reevaluate the circulation of the spinal cord, we are reporting the clinical and pathologic findings in a case in which a dissecting aortic aneurysm produced myelomalacia.

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Read in part before the Philadelphia Neurological Society, Nov. 28, 1947.

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1. (*a*) Shennan, T.: Dissecting Aneurysm, Medical Research Council, Special Report Series, no. 193, London, His Majesty's Stationery Office, 1934. (*b*) Weisman, A. D., and Adams, R. D.: The Neurological Complications of Dissecting Aortic Aneurysm, Brain **67**:69, 1944.

2. (*a*) Weisman and Adams.[1b] (*b*) Kalischer, O.: Aneurysma dissecans der Aorta mit Paraplegie, Berl. klin. Wchnschr. **51**:1286, 1914. (*c*) Reitter, K.: Aneurysma dissecans und Paraplegie, Deutsches Arch. f. klin. Med. **119**:561, 1916.

REPORT OF A CASE

C. R. W., a white man born in 1894, was admitted to the medical service of Dr. O. H. Perry Pepper in the Hospital of the University of Pennsylvania on Jan. 22, 1945. The recording of exact dates in this man's history was possible because of his wife's diary, in which she noted his symptoms. He had been in good health until the summer of 1939, when he was in an automobile accident and sustained fractures of six of his ribs on the right side. He was unconscious for about twenty-four hours after the injury. His recovery was rapid and uneventful.

He was first found to have hypertensive vascular disease in 1940, after he had a transitory episode of "drowsiness" and weakness of the right upper extremity. On Dec. 26, 1941, he suddenly collapsed while at work; his speech became thick, and the right corner of his mouth drooped. Again, he recovered in a short time.

On July 13, and again on Nov. 26, 1944, he experienced brief episodes of severe abdominal pain associated with profuse perspiration. Then, on December 27, another transitory episode of weakness of the right upper extremity occurred. On Jan. 14, 1945, he vomited his evening meal and began to have severe vertiginous attacks accompanied with sweating and nausea. These episodes occurred with increasing frequency and severity, until finally, on January 20, a severe spell was accompanied with numbness of the left wrist, the left side of his face and his left lower extremity up to the knee.

Physical Examination.—On admission to the hospital he was cheerful, cooperative and mentally alert. His blood pressure was 270 systolic and 160 diastolic. The peripheral arteries were beaded and tortuous. No arterial pulsations could be obtained in the legs below the femoral arteries. The optic fundi revealed a moderately advanced hypertensive retinopathy. The heart was enlarged, and a blowing systolic murmur was heard over the whole precordium. The liver was smooth and tender and extended 3 to 4 cm. below the costal margin.

Laboratory Studies.—The blood count was normal except for leukocytosis, with a count of 11,000 leukocytes per cubic millimeter. Renal abnormality was evidenced by albuminuria, cylindruria and marked loss of ability to excrete phenolsulfonphthalein (excretion, 2.5 per cent in fifteen minutes), a blood urea nitrogen of 21 mg. per hundred cubic centimeters and a urea clearance of 49 per cent. The serologic test for syphilis gave a negative reaction. The cerebrospinal fluid was under a pressure of 310 mm. of water, contained 59 mg. of protein per hundred cubic centimeters and presented a colloidal gold curve of 0000000000. An enlarged heart was observed on roentgenologic examination, and the electrocardiogram gave evidence of hypertrophy of the left ventricle. The old sites of fracture of the sixth, seventh, eighth and ninth ribs on the right side were noted in the roentgenogram of the chest. An intravenous urogram revealed evidence of pyelonephritis on the left side. Roentgenographic study of the gastrointestinal tract revealed evidence of gastritis with superficial ulceration in the prepyloric area. A roentgenogram of the skull showed no evidence of increased intracranial pressure, and the calcified pineal body was in normal position.

Further investigation of the circulation in the lower extremities, with use of an oscillometer, revealed blood pressures of 185 and 160 systolic and 110 and 95 diastolic in the right and left legs, respectively. The blood pressure was 255 systolic and 145 diastolic in the right arm and 265 systolic and 170 diastolic in the left arm. On fluoroscopic examination of the heart, Dr. Alexander Margolies noted what appeared to be an angulation of the left lateral border of the aorta at a distance of about 10 cm. from the aortic knob. This was not definite because of the spinal shadow. A roentgenogram of the chest did not demonstrate the roentgenologic

changes that have been found in certain cases of dissecting aneurysm.[3] On the basis of these observations an obstructive lesion of the aorta was suspected.

Course in the Hospital.—The patient was fairly comfortable while in the hospital. On January 31 he complained of an evanescent tight feeling in his chest. Although still weak, he was discharged on February 5.

Interval Note.—After his discharge from the hospital, the patient remained rather weak, bedfast and anorexic. He had considerable shortness of breath. He vomited on several occasions after eating. About 2 o'clock in the morning of February 21 he was awakened by a sensation of heaviness beneath the sternum. He was very dyspneic and was not able to move his body from the waist down. Hot water bottles were applied to his feet, the back of his knees and the lower part of his abdomen. By morning he had large, extensive burns in the areas to which the hot water bottles had been applied. He was readmitted to the hospital on February 21.

Examination on Readmission.—His blood pressure was 190 systolic and 140 diastolic. His oral temperature was 97.6 F.; his pulse rate was 100 per minute, and his respiratory rate was 26 per minute. The patient was pale and perspiring freely. The results of a general physical examination were otherwise the same as on his previous admission. Again, no pulses could be felt in the legs below the femoral arteries, but both lower extremities were warm and of normal color. On the other hand, pronounced abnormalities were found on neurologic examination. These were confined to the lower extremities. There was flaccid paraplegia. The perception of touch was lost below the level of the first lumbar dermatome bilaterally. Temperature, pain, vibration and position senses were absent below the level of the eighth or ninth thoracic dermatome bilaterally. All of the deep and superficial reflexes were absent in the lower limbs. The abdominal reflexes could not be adequately tested because of the burns on the abdomen. On the basis of these observations, Dr. John Frost, the intern who saw him first, made the following statement, "This is a transverse myelitis of the spinal cord, the cause of which I think is a dissecting aneurysm, the myelitis coming from occlusion of spinal arteries."

Laboratory Studies.—The essential observations at this time were leukocytosis, with a leukocyte count of 25,000 per cubic millimeter; albumin, casts, erythrocytes and leukocytes in the urine, and a blood urea nitrogen concentration of 48 mg. per hundred cubic centimeters. The Kolmer and Kline tests of the blood again gave negative reactions. The cerebrospinal fluid was clear and colorless; was under a pressure of 220 mm. of water; contained 4 red blood cells per cubic millimeter and 110 white blood cells, of which 76 per cent were segmented granulocytes, and contained 46 mg. of protein per hundred cubic centimeters. The tests for syphilis on the spinal fluid at this time also gave negative reactions, and the colloidal gold curve read 1133321100. The Queckenstedt maneuver showed no block of the subarachnoid space of the spinal cord.

Course in the Hospital.—The patient's temperature rose rapidly and remained elevated. He continued to complain of substernal oppression and dyspnea. He became progressively oliguric, and the blood urea nitrogen rose to 109 mg. per hundred cubic centimeters. The neurologic findings remained unchanged. Cheyne-Stokes respiration developed. He became comatose and died on March 12, nineteen days after his second admission.

3. Wood, F. C.; Pendergrass, E. P., and Ostrum, H. W.: Dissecting Aneurysm of the Aorta with Special Reference to Its Roentgenographic Features, Am. J. Roentgenol. **37**:437, 1932. Case no. 33091, Case Records of the Massachusetts General Hospital, New England J. Med. **236**:327, 1947.

General Pathologic Study (Dr. Joseph Snyder and Dr. W. F. Shelden).—Necropsy was done three hours after death.

The aorta was dilated from the aortic arch to the renal arteries. This enlargement was uniform except for a saccular bulge, about 4 cm. in diameter, which protruded anterolaterally from the right aortic wall and extended from the sixth to the eighth thoracic vertebra. The sacculation contained adherent clot, which extended into the lumen of the aorta, almost completely occluding it, and down into the renal arteries. From the sacculation there was extensive dissection of the aortic wall, extending upward to the left subclavian artery and downward to just below the renal arteries, although the renal arteries themselves were not dissected (fig. 1). The process involved from one half to two thirds of the circumference of the aorta posteriorly and included the origins of the intercostal arteries on both sides. Many of the intercostal arteries seemed to be torn off, and their lumens were thrombosed. The left renal artery was completely thrombosed. The orifice of the right renal artery was partly occluded by the thrombus extending down from the sacculation. The main dissection contained well organized thrombi at the top and bottom, and

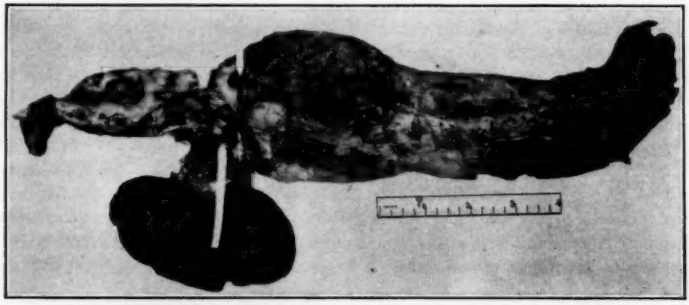

Fig. 1.—Photograph of the aorta, opened anteriorly. The arch and thoracic and abdominal portions are shown, with the left kidney. The main dissecting aneurysm, which extends from the arch to the renal arteries, can be seen in the thoracic region, where a portion of the aortic wall has been cut away. The white arrows mark the renal arteries, both of which are narrowed by the dissection and by mural thrombi. The left kidney shows the old, deep scars of previous infarction. On the left of the picture, above the renal arteries, is the large saccular bulge, with a mural thrombus on its intimal surface. A larger piece of thrombus, which projected into the lumen, has been removed.

in other portions there were recent clot formations. A small, old dissection, measuring 2 by 2 cm., was observed just above the left renal artery. There were also several separate ulcerations with thrombi, which appeared to be small dissections.

Other significant gross findings were the burned areas over the abdomen and in the popliteal spaces, where hot water bottles had been placed on anesthetic areas; an encroachment on the right pleural cavity by an inward-extending, solid, bony deformity of the sixth, seventh, eighth and ninth ribs (the result of his rib fractures) about 3 cm. from the vertebral column, and extending to within a few centimeters of the saccular bulge of the aorta; a greatly enlarged heart with patent but sclerotic coronary arteries, and both old and recent infarcts in the kidneys.

Histologically, the dissection was in the outer layers of the media, in places reaching the adventitia. A variety of changes were seen in the media, including

slight mucinous degeneration of muscle and necrosis and fragmentation of elastic fibers. The intima was irregular and contained cholesterol crystals and a few calcium deposits.

The small arteries and arterioles in many organs showed hyaline necrosis of the media. Changes in the kidneys were consistent with advancing hypertensive vascular disease and healed pyelonephritis. The other viscera presented moderate passive congestion.

Neuropathologic Studies.—Thin, brittle plaques of calcium were scattered irregularly in the arachnoid of the spinal cord. The vessels of the surface of the cord were congested throughout. The contour of the spinal cord was not altered. On palpation, the spinal cord felt soft below the emergence of the eleventh thoracic nerve roots.

On sectioning the cord in the upper thoracic regions, the usual anatomic structures were noted. At the level of the seventh thoracic nerve root there was a pale, soft area in the posterior column near the posterior commissure. As sections were made farther down, the necrotic areas appeared larger, and the usual structural landmarks were destroyed. From the area of the eleventh thoracic nerve root down to the conus the cord had a pale, thick creamy texture and was devoid of the normal internal markings.

Microscopic sections of the spinal cord were made at various levels from the second thoracic segment down to the conus. At the level of the emergence of the third thoracic nerve roots there was no definite demyelination, although there was a slight spongy appearance about the periphery of the spinal cord. The neurons were intact. The root fibers were well myelinated. The blood vessels on the surface and within the cord were full of blood.

At the sixth thoracic level more definite destructive changes had occurred. There was an irregular demyelinated area at the base of the posterior columns, between the posterior horns. One anterior horn was destroyed and contained no neural elements (fig. 2*A*).

At the eighth thoracic level the gray matter was totally destroyed on both sides. There was a large necrotic area in one posterior column. The white matter was more edematous and showed spotty areas of demyelination (fig. 2*B*).

At the ninth thoracic level the gray matter was again totally destroyed. The posterior columns exhibited greater areas of demyelination, as did the white matter immediately adjacent to the gray matter. Some of the roots were demyelinated. Blood vessels were patent and filled with blood (fig. 3*A*).

At the tenth thoracic level almost complete demyelination had occurred. The anterior spinal sulcus was identified, but otherwise the usual landmarks were not seen. The cord was filled with detritus, was edematous and showed evidence of gitter cell activity, especially in the central areas of the spinal cord and in areas occupied formerly by the gray matter. The roots at this level were swollen and demyelinated; yet roots of the cauda equina were well preserved. Blood vessels appeared to be full of blood, even within the cord. The pia-arachnoid was swollen but showed no cellular infiltration (fig. 3*B*).

At the lumbar levels there was total necrosis of the spinal cord. The area was filled with degenerated material, a few vessels and many gitter cells. The roots which arose from these levels seemed to be demyelinated and swollen; yet the fibers which came up as part of the cauda equina seemed to be intact. Blood was noted in the vessels on the surface of the spinal cord (fig. 4*A*).

In the sacral region there was a large central area of necrosis. The gray matter was destroyed. The peripheral areas of the cord remained relatively intact. The roots of the cauda equina were well myelinated. The leptomeninges were normal. Blood vessels contained blood (fig. 4*B*).

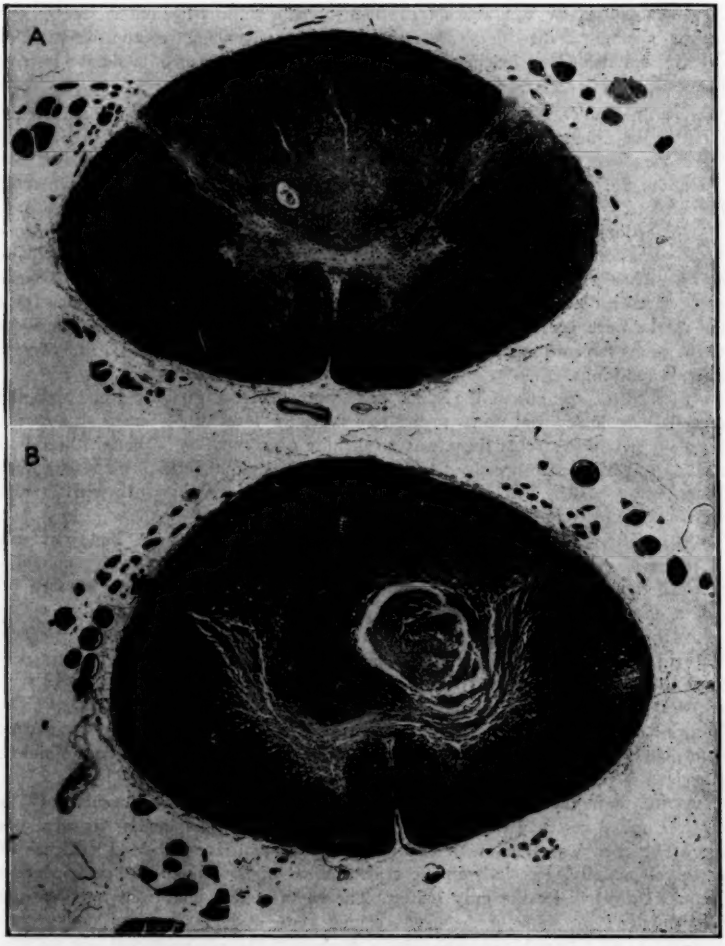

Fig. 2.—*A*, section of spinal cord at the sixth thoracic segment. Note necrosis at the base of the posterior columns with a small cavity on one side. *B*, section of spinal cord at the eighth thoracic segment, showing more extensive destruction involving the gray matter, slight swelling of the cord and a large necrotic cavity in one posterior column. Pal-Weigert stain; × 40.

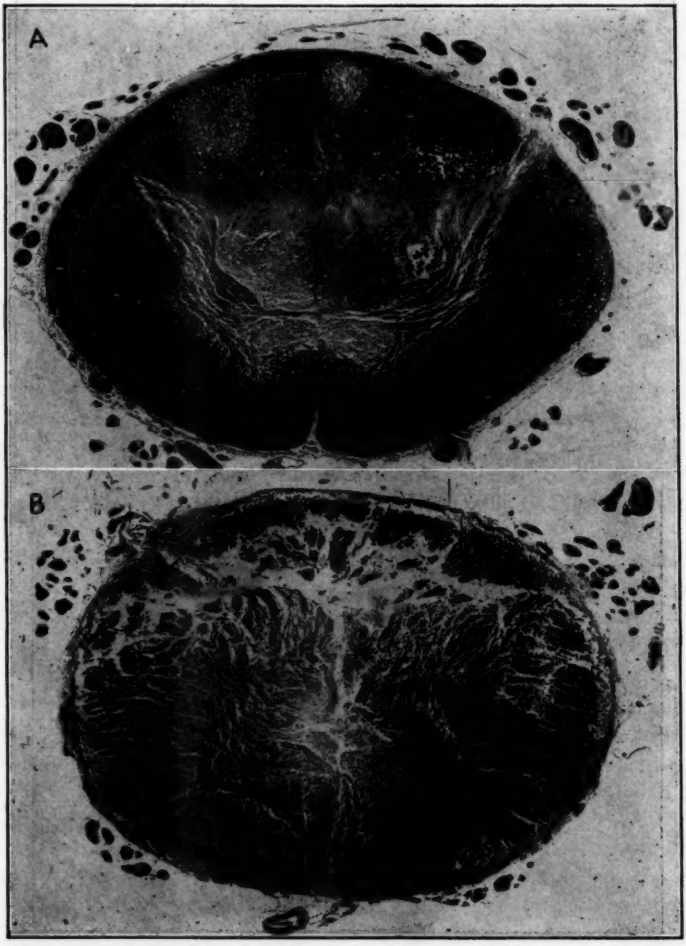

Fig. 3.—*A*, section of spinal cord at the ninth thoracic segment. More extensive necrosis is evident. *B*, section of spinal cord at the tenth thoracic segment. Total necrosis of cord is seen here for the first time. Pal-Weigert stain; × 40.

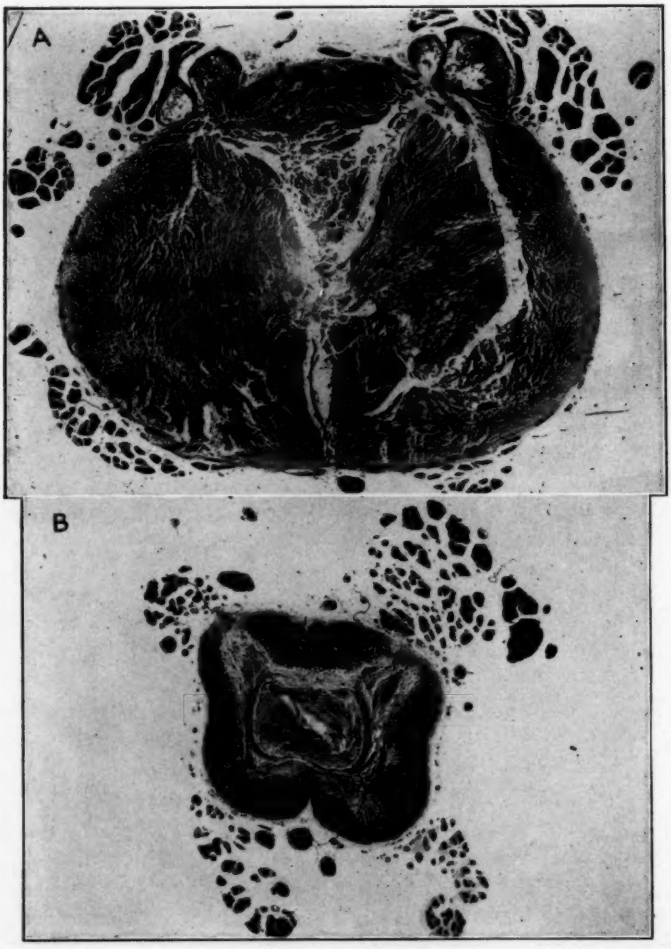

Fig. 4.—*A*, section of spinal cord at first lumbar segment, showing total necrosis. Swelling of the cord and the posterior nerve roots is seen here. *B*, section of spinal cord in the sacral region. Note the extensive central necrosis. Pal-Weigert stain; × 40.

COMMENT

General Considerations.—We feel that this case can be added to those in the literature in which the correct diagnosis of dissecting aneurysm of the aorta was made prior to death. This diagnosis is much more frequently established during life now than in 1934, when Shennan [1a] reported 300 cases, in only 6 of which the diagnosis had been made ante mortem. On the first admission of our patient, several clinicians suggested the presence of an aneurysm because of the impaired circulation in the legs. On his second admission the general clinical picture, including the neurologic and renal observations, allowed the diagnosis of dissecting aortic aneurysm to be generally entertained.

It is not the purpose of this paper to discuss the mechanism of origin of dissecting aneurysm. However, three points in this regard deserve comment in relation to our patient: 1. He had an arterial hypertension of at least five years' duration. Most patients with dissecting aneurysm of the aorta have such a preceding increased blood pressure. 2. He had sustained a severe injury to the chest six years prior to his death. Trauma, often a number of years before the onset of dissection, has appeared to be of etiologic significance in certain cases. Samson [4] found 100 cases of dissecting aneurysm of the aorta due to trauma in the literature and added 3 of his own. 3. Microscopic examination of the aorta revealed abnormalities of the media. Whether these changes represent medionecrosis cystica or resulted from loss of blood supply when the dissection occurred is not certain. Actual cyst formation, as described by Erdheim [5] and further reported by Moritz [6] and Roberts,[7] was not observed.

The commonest cause of death in this vascular disorder is sudden rupture of the aneurysm, often into the pericardial sac. Our patient pursued the more uncommon course in dying of uremia due to thrombus formation in the renal arteries.

It is a matter of conjecture as to when the dissection began in this case. If the episodes of abdominal pain in July and November 1944 were due to this process, the lesion may be presumed to have been present for at least eight months before death. That the process had been going on for a considerable time is evidenced by the presence of the small, old dissection in the aorta just above the orifice of the left renal

4. Samson, P. C.: Dissecting Aneurysms of the Aorta, Including the Traumatic Type: Three Case Reports, Ann. Int. Med. **5**:117, 1931.

5. Erdheim, J.: Medionecrosis Aortae idiopathica, Virchows Arch. f. path. Anat. **273**:454, 1929.

6. Moritz, A. R.: Medionecrosis Aortae Idiopathica Cystica, Am. J. Path. **8**:717, 1932.

7. Roberts, J. T.: Medionecrosis Aortae Idiopathica Cystica, Am. Heart J. **18**:188, 1939.

artery and the fact that in the main dissection some areas of the thrombus were well organized. Rogers [8] reported a patient who survived twenty-seven months after the initial dissection. Cases of so-called healed dissecting aneurysm have been reported, the patients dying of some unrelated cause. In these cases a rupture back into the lumen of the aorta usually occurs, thus producing a double-barreled aorta.

Clinical Neurologic Considerations.—Neurologic symptoms and signs are apparently not infrequent in cases of dissecting aortic aneurysm. In 45 of Shennan's [1a] 300 cases and in 11 of the 38 cases studied by Weisman and Adams [1b] there were neurologic disturbances. Some authors include the neurologic changes in the clinical syndrome of aortic dissection and emphasize their presence as assisting in the antemortem diagnosis. Of course, when death is rapid or when severe shock or prolonged loss of consciousness is present, the neurologic changes may be missed or ignored in the face of the intense vascular emergency.

The clinical neurologic disturbances in dissecting aortic aneurysms are the result of loss of the blood supply to the peripheral nerves, to the spinal cord or to the brain. Obviously, the clinical pictures will differ in each instance. The most frequent complication is due to ischemic necrosis of peripheral nerves. In such a case one finds paralyzed lower extremities which are cold, pulseless and areflexic and present a peripheral pattern of sensory impairment or loss. In involvement of the cord there is a flaccid, areflexic paraplegia with sphincteric paralysis and a segmental sensory loss. Since the rare cerebral involvement is due to the interruption of the circulation of the common carotid artery, the clinical picture includes flaccid hemiplegia with hyporeflexia; hemianesthesia; aphasia, if circulation to the dominant hemisphere is interrupted; ipsilateral blindness with retinal pallor, and disturbances in the state of consciousness, varying from obfuscation to profound coma.

In our case there were a number of transient neurologic incidents in the patient's life preceding his admission to the hospital. We did not feel that these were related to the dissection. The possibility that they were multiple emboli was considered. However, the neurologic disturbances were so evanescent that it seemed hardly likely that they were the result of emboli arising from the aortic clot. We felt that they represented temporary focal interruptions of cerebral function secondary to the hypertensive vascular disease.

Neuropathologic Considerations.—Of interest to us was the finding of thin, brittle, calcareous plaques in the arachnoid membrane of the spinal cord. Herren [9] found them grossly in 76 per cent of 25 con-

8. Rogers, H.: Dissecting Aneurysm of the Aorta, Am. Heart J. **18**:67, 1939.

9. Herren, R. Y.: Occurrence and Distribution of Calcified Plaques in the Spinal Arachnoid in Man, Arch. Neurol. & Psychiat. **41**:1180 (June) 1939.

secutive routine autopsies. In his study, neither the age of the patient nor the general systemic deposition of calcium could be correlated with plaque formation in the arachnoid membrane of the spinal cord. Elsberg [10] considered them harmless. In our case, we feel that they were probably a coincidental finding and were not related etiologically to the myelomalacia.

There was nothing unusual about the microscopic appearance of the softening of the spinal cord. Reparative processes were active, but the intense destructive elements still occupied the major portion of the microscopic scene. The softening began in the midthoracic region of the spinal cord and involved chiefly the posterior columns in that area. Total destruction of the spinal cord was present in the lower thoracic areas and in the lumbar portion of the cord. Central necrosis was present in the sacral region of the cord. Of considerable interest is the fact that the caudal roots were remarkably uninvolved throughout. The blood vessels of the spinal cord showed little change, and most blood vessels outside of and within the spinal cord showed the presence of blood, even in the necrotic areas.

It is of utmost significance to correlate this vast destruction of the spinal cord with the aneurysmal dissection. To do this, one must first review the circulation of the spinal cord. Kadyi,[11] Suh and Alexander [12] and Tureen [13] have contributed most to knowledge of this subject. The following description is based on their observations.

The subclavian arteries give rise to the vertebral arteries, the deep cervical arteries and the superior intercostal arteries, which supply the cervical portions and the first two thoracic segments of the spinal cord. The aorta gives rise to the intercostal arteries and the lumbar arteries, which supply the last ten thoracic segments and the lumbar and sacral segments of the spinal cord. The iliac arteries give rise to the iliolumbar arteries and the lateral sacral arteries, which supply the roots of the cauda equina. The last two lumbar arteries supply the cauda equina and send no supply to the cord itself.

From the posterior aspect of the aorta arise the paired intercostal and lumbar arteries. The intercostal or lumbar artery bifurcates, and its posterior branch gives rise to the spinal artery. The spinal artery then divides into three vessels, two of which supply ligaments, muscular elements and bony elements of the vertebral column. The third branch

10. Elsberg, C. A.: Diagnosis and Treatment of Surgical Diseases of the Spinal Cord and Its Membranes, Philadelphia, W. B. Saunders Company, 1916.

11. Kadyi, H.: Ueber die Blutgefässe der menschlichen Rückenmarkes, Lemberg, Gubynowicz & Schmidt, 1889.

12. Suh, T., and Alexander, L.: Vascular System of the Human Spinal Cord, Arch. Neurol. & Psychiat. **41**:659 (April) 1939.

13. Tureen, L. L.: Circulation of the Spinal Cord and Effect of Vascular Occlusion, A. Research Nerv. & Ment. Dis., Proc. (1937) **18**:394, 1938.

is the lateral spinal artery, which enters the vertebral canal and, in turn, bifurcates to form the anterior radicular artery and the posterior radicular artery. As its name implies, the anterior radicular artery follows the anterior spinal root to the spinal cord. On the ventral surface of the spinal cord, the anterior radicular arteries divide into ascending and descending branches, which unite above and below to form an intersegmental arterial system, known as the anterior spinal artery. This lies in the midline, in front of the anterior spinal sulcus. The posterior radicular arteries branch similarly and form a posterior intersegmental arterial system, the posterior spinal arteries. There are two of these, one on each side, in the posterolateral sulcus. These three main intersegmental arterial systems give rise to branch arteries, which form a plexus about the surface of the spinal cord. It has been found that the anterior spinal artery supplies the anterior columns, most of the lateral columns, the anterior horns and the lateral horns. The posterior spinal arteries give rise to penetrating arteries which supply the posterior columns of the spinal cord and most of the posterior horns.

It has long been understood that two arteries arise from the vertebral arteries in the upper cervical portion of the cord or the lower portion of the medulla, which unite on the ventral surface of the spinal cord to form the uppermost limit of the anterior spinal artery system. This is continuous thereafter down the entire length of the spinal cord, in an irregular fashion, with the other anterior spinal arteries, which are formed by the branchings of the anterior radicular arteries. The posterior spinal artery system begins also as branches from the vertebral arteries and is continuous down the entire cord with the union of the various segmental posterior radicular arteries.

While this arrangement would seem to give an adequate and satisfactory blood supply to the cord through an arterial system arising from above via the vertebral arteries and from below through the intercostal and lumbar arteries, such is not actually the case. Kadyi [11] noted that even though each lateral spinal artery divided into an anterior and a posterior radicular artery, usually only one of these branches was adequately developed at any given segment. Sometimes both radicular arteries were so small that they merely supplied the nerve roots they accompanied. Indeed, in only a few instances did one lateral spinal artery give rise to both radicular arteries. In the average human spinal cord, only every second spinal root between the second cervical segment and the third lumbar segment was accompanied with radicular arteries, and even this arrangement was not of equal or regular distribution. The spinal cord of man contained from 15 to 34 radicular arteries. Two to 17 of these were anterior, and 11 to 23 were posterior. In the average spinal cord there were only 8 anterior radicular arteries and 17 posterior radicular arteries. The more abundant the arteries, the smaller was their caliber.

Between the eighth cervical segment and the ninth thoracic segment of the spinal cord, usually only two small anterior radicular arteries were found. A large artery, the great anterior radicular artery, was usually observed on one side accompanying a spinal root between the ninth

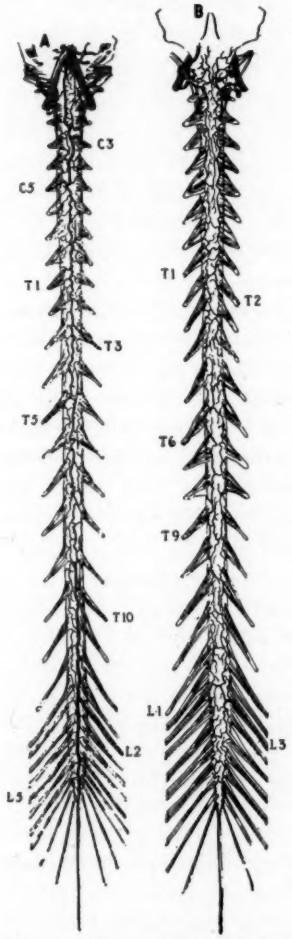

Fig. 5.—Drawing of the arterial supply of the spinal cord and spinal roots (*A*, ventral view; *B*, dorsal view), taken from Suh and Alexander.[12] Note especially the large anterior radicular arteries at the tenth thoracic and second lumbar roots on one side, whereas the other anterior radicular roots in the thoracic region are very much smaller or are absent.

thoracic root and the third lumbar segment (fig. 5). This important artery was usually formed at the tenth thoracic segment or the first or second lumbar segment.

Anatomically, therefore, the cervical and the lower thoracic-lumbar-sacral segments of the spinal cord seem to be well supplied with arteries. The thoracic portions (upper and middle) of the spinal cord have the poorest segmental supply, but they anastomose above and below. Such anatomic findings must be evaluated from a functional point of view. Tanon [14] injected the arteries of the spinal cord at various levels. From the lumbar vessels, he was able to inject the arterial tree of the whole spinal cord with ease. Above the ninth thoracic segment, only short areas of the spinal cord could be injected through one segmental branch. In the cervical portion of the cord, injection of a root artery was again a rather localized affair. In the light of such observations, it would seem that the arterial supply through the lumbar portion of the spinal cord must be of utmost importance for a great portion of the spinal cord, especially the thoracic.

Observations on experimental aortic obstruction at first yielded rather contradictory information concerning ischemia of the spinal cord.[15] However, Tureen [13] has shown that clamping the aorta of cats below the arch did lead to complete interruption of the circulation of the spinal cord below the lower thoracic segments. Ischemia of fifteen minutes' duration resulted in reversible functional and histologic changes in the spinal cord. Ischemia of more than twenty minutes resulted in permanent disturbances in the structure and functions of the spinal cord.

On clinicopathologic grounds, too, at first, aortic obstruction was thought not to produce ischemic softening of the spinal cord.[16] Kahler [17] stated the belief that the collateral circulation of the spinal cord from the cervical spinal arteries would prevent softening, even with the thoracic aorta obstructed. He concluded that the clinical findings were the result of the ischemia on the peripheral nerve endings, both motor and sensory, and not on the cord or the peripheral nerves. Rogers [8] also expressed the opinion that the collateral circulation of the spinal cord was too abundant to allow the development of an ischemic necrosis of this structure.

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14. Tanon, L.: Les artères de la moelle dorsolumbaire, Thesis 98, Paris, 1908; Paris, Vigot Frères, 1908.

15. Tureen,[13] p. 416.

16. Schlesinger, H.: Ueber Sensibilitätsstörungen bei akuter lokaler Ischämie, Deutsche Ztschr. f. Nervenh. **29**:375, 1905. Drăgescu, R., and Petrescu, M.: Contribution à l'étude de la pathogénie de la paraplégie consécutive à la thrombose aortique, Bull. et mém. Soc. méd. d. hôp. de Bucarest **11**:243, 1929; abstracted, Zentralbl. f. d. ges. Neurol. u. Psychiat. **56**:540, 1930.

17. Kahler, H.: Ueber Störungen des Nervensystems bei arterieller Ischämie, Wien. klin. Wchnschr. **47**:1186, 1934.

Kalischer [2b] and Reitter,[2c] however, each reported a case of softening of the spinal cord proved by pathologic study. Kalischer's patient was a 66 year old locksmith whose aortic dissection occurred on a Friday evening. He succumbed Sunday morning. He had complete paralysis of his lower extremities. A dissecting aneurysm of the thoracic aorta was noted to have torn off the fourth, fifth, sixth, seventh and eighth intercostal arteries on both sides. The ninth and tenth intercostal arteries were shorn off on the left side only. Some ischemic changes were noted in the dorsal portion of the thoracic region of the spinal cord. The neurons of the spinal cord were intact, a condition which Kalischer ascribed to the short duration of the patient's life after the dissection.

Reitter's case is particularly instructive. The dissecting aneurysm occluded the first eight pairs of intercostal arteries. His patient had a flaccid areflexic paraplegia and loss of all sensation below the lower part of the abdomen. The spinal cord showed ischemic necrosis from the sixth thoracic segment down into the conus. The posterior columns were somewhat spared, although the rest of the cord was considerably damaged. Weisman and Adams'[1b] patient also had a flaccid areflexic paraplegia. Loss of pain and temperature senses with preservation of touch, vibration and position senses was demonstrated below the eighth thoracic segment. An ischemic necrosis of the anterior portions of the spinal cord was observed below the fifth thoracic nerve root. Here, too, the posterior columns were rather well preserved. A dissecting aortic aneurysm was found to have "shorn" the intercostal arteries from the aorta on both sides.

These 3 cases and our case would seem to indicate that in certain circumstances ischemic necrosis of the spinal cord can occur with a dissecting aortic aneurysm, contrary to the speculations of Kahler, Rogers and others. All the factors involved in such infarctions may not be clear as yet. The spinal cord can be seriously injured if the upper intercostal arteries are severed, as shown by the cases of Kalischer, Reitter, and Weisman and Adams; it can be totally destroyed if the lower intercostal and upper lumbar arteries are also involved, as in our case. The actual histopathologic changes are also dependent on the duration of survival after the onset of the ischemia. Tureen noted chromatolysis beginning seven hours after establishment of ischemia. Thirty-six hours after the onset of disturbed circulation, interstitial changes became evident. Our patient survived nineteen days after the onset of the lesion in the cord; this probably accounts for the extensive changes in the cord which we observed. If death occurs too soon after the dissection, little or no change in the structure of the spinal cord may be expected. Such factors may have accounted for previous differences of opinion on this subject.

CONCLUSIONS AND SUMMARY

A case of dissecting aneurysm of the aorta is reported, in which the diagnosis was made before death.

The clinical neurologic picture of a transverse lesion of the spinal cord was found to be due to myelomalacia.

The arterial circulation of the spinal cord is reviewed anatomically and physiologically to explain the occurrence of myelomalacia. The conclusion seems justified that in certain circumstances the apparently anatomically adequate arterial system of the spinal cord may be functionally inadequate. Some of the factors involved in this vulnerability are discussed.

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MANIC PSYCHOSIS IN A CASE OF PARASAGITTAL MENINGIOMA

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THE ADVANCES in the field of pneumoencephalography and electroencephalography have considerably facilitated the diagnosis of tumors of the brain. Nevertheless, every physician, particularly the neurologist and the psychiatrist, knows how easily the diagnosis of a brain tumor may be overlooked. This is particularly so when there are few or no neurologic symptoms or when the symptoms are of a neurotic or psychotic nature. Particularly, the initial symptoms may be those one finds in a neurotic person. Cohen [1] described the case of a sailor who was surveyed out of naval service for a variety of neurotic symptoms, particularly anxiety attacks and numerous somatic complaints. Only forty months after the onset of the symptoms the diagnosis of a large astrocytoma was made. The difficulty in making the diagnosis of brain tumor is due largely to the fact that there is no symptomatic picture which may be considered characteristic of a tumor of the brain, and particularly that the mental symptoms accompanying such a tumor are manifold. Of course, certain psychiatric symptoms are characteristic of involvement of certain areas—for instance, for tumors of the frontal lobe, euphoria, witzelsucht, silliness, memory defects and slowly progressive deterioration; for tumors of the temporal lobe, olfactory and gustatory hallucinations, together with epileptiform attacks, and for tumors of the occipital area, certain visual hallucinations and optic disturbances. Nevertheless, these, and similar, symptoms sometimes may be found with tumors of other areas, and there may be other symptoms. Jameison and Henry,[2] in their extensive study of mental aspects of tumors of the

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1. Cohen, L. A.: Astrocytoma of the Left Cerebral Hemisphere, with Psychoneurotic Reaction, M. Bull. Vet. Admin. **20**:94 (July) 1943.

2. Jameison, G. R., and Henry, G. W.: Mental Aspects of Brain Tumors in Psychotic Patients, J. Nerv. & Ment. Dis. **78**:333 (Oct.); 500 (Nov.) 1933.

brain, emphasized the difficulty of diagnosing such a condition because of the variety of psychotic symptoms accompanying a cerebral tumor. They stated that if it were possible to describe a psychosis which is peculiar to cerebral tumor it would undoubtedly have been done long ago. This statement, which they made seventeen years ago, is still true.

Mental pictures which accompany a brain tumor may simulate the most varied forms of psychoses. One sees pictures of delirium and confusion—symptoms which might be found in any organic disease of the brain—the Korsakoff syndrome, symptoms resembling those of dementia paralytica, varieties of depressive features and, finally, schizophrenic-like symptoms. There is one picture, however, which appears to be extremely rare and of which only a few cases have been reported in the literature, namely, that of a typical manic psychosis. I was unable to find any case of a manic psychosis accompanying a parasagittal meningioma. The case which is presented here went for years under the diagnosis of epilepsy. Even when the manic picture first appeared, the correct diagnosis of a tumor was not made.

REPORT OF CASE

A veteran aged 29, married, was admitted to the Veterans Administration Hospital, Perry Point, Md., on July 6, 1949. The admission papers stated that he had been under treatment for epilepsy and had been taking 3 tablets (65 mg.) of phenobarbital, 3 tablets (100 mg.) of mesantoin® (3-methyl-5-phenyl-5-ethyl hydantoin) and 1 capsule (100 mg.) of diphenylhydantoin sodium daily. For several months prior to admission he had had increased psychomotor activity and emotional lability. At the time of admission he was very talkative, easily distractible and restless, looking around the office and repeating the names of common objects to himself. He stated that he was suffering from epilepsy and was very anxious to receive help. However, later, when asked what his complaint was, he said, "Nothing, sir, just ignorance; just gross ignorance of the people around here."

The patient's father died of cirrhosis of the liver when the patient was 17 years old. The mother, aged 69, was alive and in good health. There were 4 brothers and 2 sisters, all apparently in good health. No neuropathic traits had appeared in any member of his family.

The patient's birth and early development were normal. He began school at the usual age and got along except in mathematics, which he found detestable. He himself stated that the only unusual thing in his development was that he was more sensitive than most people, that he enjoyed reading and that he liked to be alone as much as with people. He felt that he had an artistic tendency, which had always remained. At the age of 17, when he was a senior in high school, his education was interrupted by the death of his father. At that time he began to drink heavily and spent much time away from home. He got a job with a steel company and worked there at various jobs from 1936 to 1941, at which time he was inducted into the Army. He felt that he got along well in his employment. Again, he did not like the mathematics involved in his work with the sheet metal section. At that time his drinking became a more serious problem. He even came to work while under the effects of alcohol. He was not alert to the job and said that he simply did not care. In spite of being somewhat seclusive, he sought out people, particularly about the

time that he began to drink. He dated a number of girls and felt that he always got along very well with people. In his own attempt to review his early history, he decided that he had always been a highstrung person.

On induction into the Army, he served as a rifleman, became a supply sergeant and drank heavily on his time off. He stated that his job as a supply sergeant made him very nervous and entailed a great deal of responsibility. He was under the pressure of activity, working with the units which were being broken up to go overseas. He continued his drinking and confided that he was going so strong day and night that the tension had to "break." In 1943 he had the first attack of unconsciousness. One morning, while in the supply officer's office, he suddenly experienced a peculiar sensation. His muscles tensed, and he became very nervous. His hip and back tended to draw to the left. His body slid to the floor, and he became unconscious. He woke up in the dispensary. He did not know whether he had tonic or clonic convulsions or whether he was rigid. He was kept under observation for epilepsy. Later, while at Fort Knox, he had another attack. There was some question about a release from service at that time, to which he would not consent. At that time (Aug. 4, 1944), he had a neuropsychiatric consultation. The psychiatrist stated that, in his opinion, without proof, the patient was potentially epileptic and that his attacks were precipitated by alcohol. Essentially normal laboratory findings and an unconvincing electroencephalogram, together with the consultant's impression that the patient was extremely capable, well trained and anxious to receive advice, influenced him to make the diagnosis of syncope, cause undetermined; and it was recommended that the patient be sent overseas. At that time he promised to stop drinking. He was overseas for eleven months. Finding that he had no subsequent attacks, he was happy, despite his being in heavy combat. He resumed his heavy drinking and found that he had no more attacks. However, he became rather tense. He returned to the United States, at which time he was discharged. He was not clear about the exact basis for his discharge from the service but claimed that it was a neurosis. According to the claims file, he received an honorable CDD on Oct. 12, 1945, and later 50 per cent compensation was awarded on the basis of a neurosis.

After his return from the service, he lived at home with his mother and one of his brothers. He went to work as storekeeper in a warehouse in November 1945. He had had one epileptic attack prior to this employment; after working there ten months, without any noticeable difficulties, he had another attack. Information, dated Oct. 21, 1946, stated that he had not been getting along well on the job and that he had received a bad efficiency rating. He brought the matter to a higher board, and the efficiency rating was changed from unsatisfactory to fair. Finally he was moved to another warehouse, under a different foreman. He continued to work there as a civil service employee until about a month prior to his admission to Perry Point.

The patient was married on April 7, 1948, and the couple had one child. He continued, however, to live in the home of his mother, whom he supported almost entirely. She did not want him to move away from her; once, when he said that he was going to leave, she threatened to take poison. She was said to be domineering and to have objected to the patient's marriage. This home situation apparently put a considerable strain on the patient.

When seen in the mental hygiene clinic of the Veterans Administration in 1946, the patient was concerned about his seizures and decided to go to the hospital to seek help. He was dissatisfied with the interview which he had with the physician there. He then went to another physician, who recommended phenobarbital. However, the doctor doubted whether his attacks were really epileptic and advised the

patient to lead a more normal life. The patient again was doing a great deal of drinking and was going out nights to the extent that he did not get the proper rest. He finally went to another physician, but again no specific diagnosis was made. This fact upset him quite a bit. When he had the attack in September 1946, which was preceded by an aura, he related this seizure to his worry about his efficiency rating. At that time, he had three attacks on three consecutive days. All three occurred in the evening. A witness stated that he twisted, turned, bit his tongue, then became relaxed and slept. At that time he started to visit a chiropractor, who stated that the patient was probably not epileptic; after taking a roentgenogram of the patient's skull, the chiropractor stated the belief that here was some pressure, which might be relieved through treatments. It is not clear of what nature these treatments were.

On Oct. 24, 1946, a psychiatrist at the regional office of the Veterans Administration recommended that the patient have a pneumoencephalographic examination and be referred to the mental hygiene clinic because of personality difficulties. The psychiatrist expressed the belief that the patient was epileptic. An electroencephalogram was reported as being consistent with a diagnosis of epilepsy. A pneumoencephalogram apparently was not made.

In the succeeding years, the patient was seen in the mental hygiene clinic of the Veterans Administration. There the impression was that the patient had epilepsy, perhaps influenced to a considerable degree by chronic addiction to alcohol since the attacks seemed to be more frequent when he went on heavy alcoholic sprees. However, throughout the course of his visits, he gave up alcohol entirely. He showed a sincere desire to help himself. With the medication which was given him, epileptic seizures were reduced almost to a minimum. Further electroencephalographic records did not show any change and continued to be consistent with epilepsy. It was the impression, however, that his marriage had initiated tension and had increased the frequency of his seizures. During the first half of 1949 he had several attacks, whereas prior to this months would go by without an attack. He continued to receive medication and occasional psychotherapeutic interviews to relieve his anxiety over these attacks.

During the Easter season of 1949, while still visting the mental hygiene clinic, the patient showed a change. He showed evidence of hypomanic behavior, and there was flight of ideas. He exhibited much emotional elation and increased psychomotor activity, while previously his personality was described as that of a quiet, reserved person, bordering slightly on the schizoid. He had always been a rather quiet person, who liked to read and attend movies and sports events. One day in May 1949, he suddenly burst out crying and was afraid of the light. This was apparently the first abnormal action noted by members of his family. In the following days and weeks he began to talk more and more and became very argumentative. He was belligerent toward his work and the employees there, and it was decided to give him a period of leave. He showed considerable irresponsible behavior, and it became increasingly difficult to handle him. He would come into the mental hygiene clinic at irregular hours and show decidedly irresponsible thinking; he was grossly coarse in his attitude toward the therapist, whereas before he had been respectful to every one. At that time it was believed that his marital situation, in which there was considerable tension between his wife and mother, and the pregnancy of his wife, during which she made considerable demands on him, were responsible for this acute breakdown. The patient later stated that he had a superabundance of energy during work and after work, that he got very little sleep and that something was driving and pressing him. Finally he was admitted to the Veterans Administration Hospital at Perry Point on July 6, 1949.

From the beginning of his stay at Perry Point, the patient was definitely manic. He joked and was elated, talkative and distractible. The physical examination at that time showed a condition entirely within normal limits. The neurologic examination showed that the pupils were of medium size and reacted to light and in accommodation; the fundi were normal, and the cranial nerves were not involved. The deep reflexes in the upper and lower extremities were somewhat increased but were equal on the two sides; there was no clonus; the Hoffmann sign was not elicited. A temporary Babinski reflex was present on the left side; at other times, however, the Babinski sign was absent. Abdominal and cremasteric reflexes were normal. The gait was free; there was no evidence of spasticity. Coordinated movements were slightly slower on the left side than on the right. There was no evidence of involvement of the posterior columns of the spinal cord or of the peripheral nerves. Roentgenograms of the chest revealed nothing abnormal, and roentgenograms of the skull did not show any evidence of bone erosion or of increased intracranial pressure. The serologic reactions of the blood were negative.

The patient continued to be very irritable, annoying to the other patients, demanding and difficult to handle. He accused the aides of persecuting him. A few days after admission he had a generalized convulsion of the grand mal type. He talked almost incessantly. Most of the time he was in a mood of elation but on occasion he became hostile and threatening. On some occasions he would suddenly burst into tears. He was grandiose and expansive in his ideas. He stated that he knew as much neurology and psychiatry as the average physician. Once, when he was asked what was his first occupation, he replied in a facetious manner, "I was a carpenter, like Jesus." His behavior was more and more annoying to the other patients, and it became necessary to send him to a ward for more disturbed patients. There his condition at first did not show much change. He was very critical and rather aggressive, not hesitating to tell the examiner what ideas he should have about certain matters. He expressed a general, unsystematized feeling of persecution, covering most of his stay in the hospital. At times he was somewhat depressed. He would say, "Why shouldn't I be depressed after all these years of illness?" referring to his history of seizures. His orientation was always perfect. His memory for recent and past events was good, and there was no cloudiness of the sensorium. However, his insight was seriously defective and his judgment very poor. Finally he became so noisy that it was necessary to give him hydrotherapy in the form of continuous bath and neutral packs; at other times he had to be placed in seclusion. There, isolated from his environment and no longer distracted, he quieted down and did some clay modeling. He continued to receive diphenylhydantoin and phenobarbital and had an occasional generalized seizure of the grand mal type. During August he was on the whole somewhat quieter; the picture was of the hypomaniac rather than the manic variety. Occasionally he appeared somewhat confused; the sensorium was not entirely clear. However, these states were only transient.

An electroencephalogram (fig. 1), performed on July 26, 1949, was reported as follows: "There were much low voltage, fast activity and frequent outbursts of F-1 (18 to 22 per second) and F-2 (20 to 30 per second) activity. The amplitude of the F-2 activity was higher on the left than on the right, particularly over the frontal and temporal areas. There were some sharp spike seizure discharges, particularly over the left frontal area. Sleep did not bring out any other abnormality. There was no build up on hyperventilation. The impression was that of an abnormal electroencephalogram consistent with the diagnosis of grand mal epilepsy, with a possible focus over the left side." A pneumoencephalographic study was recommended.

Prior to the pneumoencephalographic examination, another neurologic examination revealed for the first time some blurring of the margins of the disks. Studies of the spinal fluid showed moderate elevation of pressure, a cell count of 5 lymphocytes per cubic millimeter, 63 mg. of sugar and 36.6 mg. of protein per hundred

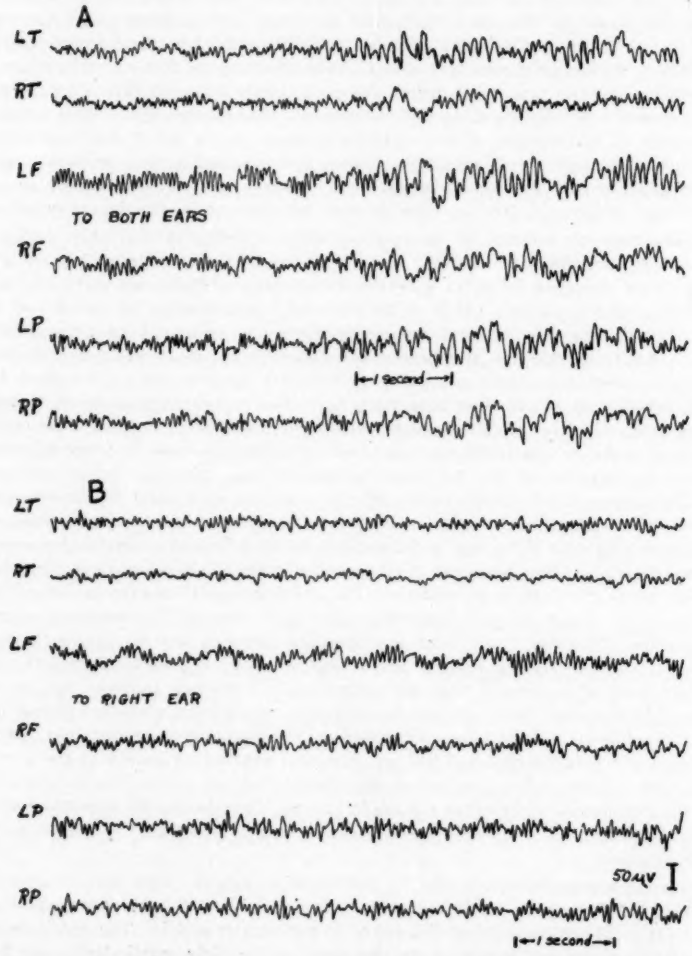

Fig. 1.—*A*, preoperative electroencephalogram, scalp to ear recording, showing F-1 activity with focal slowing over the left frontal area and some spread to the other areas. There was asymmetry of amplitude, with that on the right side lower than on the left.

B, tracing from the same record as that in *A*, showing F-1 activity.

cubic centimeters, a negative reaction for globulin, a positive reaction to the Kolmer test (32 units) and a colloidal gold curve of 1111100000.

The pneumoencephalogram, which was obtained on Sept. 1, 1949, revealed that the ventricular system was pushed to the left. The third ventricle was slightly oblique and shifted; the right lateral ventricle was cut off and markedly flattened above in a straight line. A plain roentgenogram of the skull showed some very large venous channels, more on the right than on the left, but with no definite enlargement of any part of the arterial tree. There was a suggestion over the vertex of small arteries perforating the bone. The findings in the films were interpreted as those of a parasagittal meningioma on the right side. An operation was carried out immediately.

The operation verified the findings of the pneumoencephalogram, revealing a grayish white tumor in the right frontoparietal area. The tumor was not adherent to the dura except in a very small area. There was considerable bleeding during the operation. The tumor was removed with the exception of fragments at the point of its attachment to the falx, the removal of which was postponed until later. The tumor weighed 74.5 Gm. and was approximately the size of a hen's egg. After the first operation the patient did very well. At the time of the second surgical procedure, on September 27, the neurologic status was essentially normal. At that time the remaining fragments of the tumor were removed as much as possible, and the necessary cauterization was done.

The patient's condition immediately following the first operation was somewhat stormy; he was relatively lethargic, with weakness of the left arm and leg. However, within several days there was a decided shift to improvement, and convalescence was rapid. He was quiet and cooperative, talking in a friendly and coherent manner. There was no evidence of overactivity or overtalkativeness. The postoperative course after the second procedure was exceedingly good and was uneventful. The patient was no longer on the psychiatric service but was kept on the surgical service after the first operation.

Pathologic examination of the tumor confirmed the diagnosis of a parasagittal meningioma. The specimen was an irregular, somewhat nodular, mass of tissue, 7 by 5 by 4.5 cm., enclosed in a capsule, firm and grossly fibrous. Microscopic examination (fig. 2) showed cells with a small, round, deep-staining nucleus and cells with a large vesicular nucleus, which was frequently multilobular. The reticulum between the cells was delicate and rather scanty. The blood vessels were numerous. The wall was rather heavy and fibrous, apparently having been present for a long time. The capillary supply was abundant, and the capillaries were not abnormal. There was a tendency for the tumor cells to arrange themselves about the large capillaries. In a few small areas the blood vessels among the tumor cells had completely degenerated, and the remaining substance was eosinophilic. Mitotic figures were not seen, but some of the nuclei had three or four nucleoli, and other nuclei appeared to have just completed cell division. The interpretation of the pathologist was meningioma showing sarcomatous changes.

During his further stay in the hospital, the patient was entirely free from epileptic seizures. He was given diphenylhydantoin and phenobarbital.

A second electroencephalogram was taken on Oct. 21, 1949, the day of his discharge from the hospital. In this second record, most of the fast activity which appeared in the first had disappeared and was replaced by a normal alpha rhythm. Outbursts of moderately fast activity were still present. There was no definite evidence of spikes. In the first record there were short outbursts of 6 to 7 per second waves, particularly on the left side, whereas the second record showed some slow activity of about 5 to 6 per second waves over the right temporal area with

spread to the right parietal area. For the rest, the amplitude was somewhat lower over the right parietal area than over the left. Sleep spindles were also less pronounced on the right.

Toward the end of his stay in the hospital, the patient was seen a few more times in psychiatric consultation. He was friendly, patient and cooperative. There was no evidence of flight of ideas or psychomotor hyperactivity. He showed good insight into his mental condition. He stated that he had had a nervous breakdown, had been afraid of light and had thought that he was going blind. He remembered

Fig. 2.—Microscopic appearance of the meningioma.

that he had talked incessantly in order to free his mind. He had gotten very little sleep. He denied having had any hallucinations or delusions. He remembered that in the hospital he was extremely overactive. Everything seemed electrical to him. The floors appeared wired, and he felt shock in his feet. He thought that he must have been confused. The hospital seemed a horrible place to him. When asked about his prepsychotic personality, he stated that he was quiet and easy-going and had several friends. His spirits were even, and he never had periods of depression or overactivity. He had worried about his epileptic spells and had become more irritable as time went on.

Psychologic testing was done shortly before his discharge. This was not possible prior to the operations because of his mental status. A Wechsler-Bellevue test showed intelligence quotients of 119, 106 and 114. It was possible to place the patient's original endowment at a superior level. Four tests for organicity revealed impairment in those areas of psychologic functioning usually affected by organic involvement. The Wechsler-Bellevue deterioration score was 29 per cent. The Babcock efficiency index was —10. These two ratios indicated that the patient's level of functioning was definitely inferior to his level of capacity. Psychologic testing revealed inefficiency in those mental functions usually impaired by organic involvement. The report went on to say: "These deficiencies are probably not severe enough to interfere with the patient's adjustment on a moderate plane. Anxiety is an outstanding factor. Emotional immaturity accompanies this anxiety in a basically neurotic structure. The patient is felt to be oriented to a paranoid type of thinking. Whether this will endure or will lose its meaning in the patient's subsequent adjustment is questionable. The patient shows a good deal of self confidence; on the other hand, he might fall back on his recent experiences and wish to be treated as a child. The outlook for the future in terms of psychologic testing is somewhat optimistic."

A neurologic examination done shortly before the patient's release from the hospital was reported on as follows: "The deep reflexes of the upper and lower extremities were increased throughout, but were equal on the two sides. There was a sustained ankle clonus on both sides, being more pronounced on the left than on the right. A Babinski sign was elicited on the left side. The left arm was slightly weaker than the right. The left nasolabial fold was somewhat weaker on the left than on the right. There was no ataxia, disturbances of gait or disturbances of sensibility. The pupils were large, round and equal and reacted to light and in accommodation; the fundi were normal."

Further psychiatric and neurologic examinations, which were done one month later, showed no further changes.

The patient returned to the hospital for a check-up four months after his discharge from the hospital. At that time his mental condition appeared entirely normal, although he had been worried about an epileptic seizure which occurred about two weeks previously. He was working at his old job but took leave after he suffered the seizure. He continued to receive anticonvulsant medication, the amount of which was increased. He showed very good insight into his mental condition. The patient realized that he had been mentally ill. Another electroencephalogram, taken at this time, continued to show abnormalities, consisting particularly of slowing of the brain waves over the right parietal and frontal areas. The patient returned home the same day.

It is evident from this description of the case that epileptic seizures of the grand mal type were the patient's only symptoms for several years. Electroencephalographic studies which were made prior to his admission to the hospital did not show any evidence of a space-occupying process, or even of an epileptic focus. There was only evidence of a generalized epileptic process. When the patient was first admitted to the hospital, the combination of epilepsy and manic psychosis was striking; because of the extreme rarity of such a combination, an organic process, differing from mere generalized epilepsy, was suspected. Therefore, studies directed toward localization were initiated, but some were delayed

because of the patient's hyperactivity. In fact, the electroencephalogram showed evidence of a focus of slow activity; therefore air studies were suggested immediately. When the patient was first seen in his manic excitement, which was a classic picture of such a psychosis, no one would have suspected, without knowing it, that the patient was suffering from epileptic seizures. All the classic symptoms of overactivity, overtalkativeness, elation, irritability, distractibility, flight of ideas and jocularity were present. There was not the euphoria or silliness one sees in cases of tumor of the frontal lobe, but there was elation.

One of the most extensive studies of mental disturbances associated with brain tumor was made by Schuster.[3] This study, made in 1902 and still considered a classic one, comprised 775 cases of brain tumor with mental symptoms. In only 13 of this series was there a manic-like picture. However, most of these 13 cases were not clearcut instances of manic psychosis. Delusions were described in 3 of them. In 1 case the manic state occurred in the puerperium. In 1 case the patient alternated between mania and apathy. In most of his cases there was impairment of intellect. Of the 13 cases, the frontal lobe was involved in 1 and the occipital lobe in 1; in most of the rest the brain stem was involved; in none was the parietal lobe affected. In conclusion, Schuster stated:

> Tumors of the brain, particularly of the frontal lobe, are rarely accompanied with a typical manic psychosis. While the picture coincides in all other aspects with that of a genuine manic psychosis, one often finds impairment of the intellect as well.

Schuster came to the conclusion that the type of mental disturbance is somewhat dependent on the location of the growth but that in general there is no picture typical of any particular type or site of tumor.

Of Knapp's[4] series of 64 cases of brain tumor, in 58 of which there were mental symptoms, none showed a manic-depressive psychosis. In only 1 case was there a picture of melancholia. Knapp concluded, like other observers, that there is no specificity for the site of tumor. In 1 of his 2 cases of tumor of the parietal lobe there was general dulness, and in the other, symptoms of a neurasthenic nature.

Davidoff and Ferraro[5] studied a large series of cases of intracranial tumors in New York state psychiatric hospitals. Like others, they observed all kinds of mental disturbances in these patients. They agreed with the other observers that there is no characteristic mental picture.

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3. Schuster, P.: Psychische Störungen bei Hirntumoren, Stuttgart, F. Enke, 1902.

4. Knapp, P. C.: The Mental Symptoms of Cerebral Tumor, Brain **29**:35 (April) 1906.

5. Davidoff, L. M., and Ferraro, A.: Intracranial Tumors Among Mental Hospital Patients, Am. J. Psychiat. **8**:599 (Jan.) 1929.

They noted the affective changes which may be present, but they did not mention the occurrence of manic psychosis. They stated the belief that a tumor might produce a potential psychosis in sensitive persons.

Henry [6] reviewed 1,000 verified cases of brain tumor, gathered chiefly from the literature. He stated that intracranial hypertension is manifested by depression, anxiety and physical distress, particularly referable to the head, alternating with somnolence or euphoria or disorientation. He concluded that certain symptoms are more or less frequent with the involvement of certain areas, but he could find no mental picture which was characteristic of any particular location of tumor.

Moersch [7] reviewed psychic changes associated with brain tumor in cases at the Mayo Clinic. He classified them into three groups: general symptoms, specific mental reactions and associated mental reactions. Among the general symptoms he noted anxiety states and depressive reactions, but he did not mention manic states. With respect to the associated reactions, he stated that hysterical episodes, maniacal states or other psychotic states which occasionally lead to institutional confinement may at times be quite independent of the effects of the neoplasm. He stated the belief that the pronounced changes brought about by a new growth in the brain are likely to precipitate psychic alterations, especially in neuropathic persons, in whom the stabilizing qualities are none too good.

Hoffman [8] stated that there is no psychosis characteristic of brain tumor and that there are no symptom groups characteristic of tumor located in a specific lobe or area. He went only so far as to say that certain mental symptoms suggest localization in one direction or the other. As regards emotional reactions accompanying brain tumor, he stated that they are variable. There were several cases with depression and 1 with pronounced euphoria and facetiousness, but, again, there was no mention of a manic psychosis or manic-like picture.

Brock and Wiesel [9] examined a small series of patients whose psychotic symptoms masked the onset of brain tumor. In 1 of these patients an agitated depression constituted the initial illness. This patient was treated with electric shock before the correct diagnosis was made.

6. Henry, G. W.: Mental Phenomena Observed in Cases of Brain Tumor, Am. J. Psychiat. **12**:415 (Nov.) 1932.

7. Moersch, L. P.: Psychic Manifestations in Cases of Brain Tumors, Am. J. Psychiat. **4**:705 (April) 1925.

8. Hoffman, J. L.: Intracranial Neoplasms; Their Incidence and Mental Manifestations, Psychiatric Quart. **11**:561, 1937.

9. Brock, S., and Wiesel, B.: Psychotic Symptoms Masking the Onset in Cases of Brain Tumor, M. Clin. North America **32**:759 (May) 1948.

These observers stated that diagnoses such as schizophrenic reaction, agitated depression and involutional psychosis might be made when actually a brain tumor was present.

Interesting observations in cases of brain tumor were made by Foerster.[10] He described a case of a suprasellar craniopharyngioma. Pressure of speech with flight of ideas, such as one sees in a manic state, developed when he (Foerster) began to manipulate the tumor during the operation. Foerster concluded that all the manic reactions displayed by the patient were strongly dependent on this manipulation and on its effects on the floor of the third ventricle. He cited a similar manic-like syndrome in a case of papilloma of the choroid plexus, in which bleeding occurred into the third ventricle during the operation. Whenever he tried to remove the blood clot and touched the floor of the third ventricle, the patient showed manic excitement. He produced ideas of grandeur and was very talkative. This patient had never shown any previous evidence of manic behavior. Foerster added that he had made similar observations so often that he no longer doubted that through mechanical irritation of the anterior section of the hypothalamus a manic-like picture could be precipitated.

The case most similar to the one reported in this paper was seen by Stern and Dancey.[11] It was that of a young woman with a glioma of the diencephalon. This patient had had a prolonged attack of mania, which increased in severity. For a long time she presented a typical picture of hypomania, flight of ideas, psychomotor overactivity and irritability. During her hospitalization, she expressed ideas of grandeur and criticized her husband for his stupidity. She became so disturbed that finally she had to be transferred to a ward for disturbed patients. Her death occurred suddenly; autopsy revealed a lesion occupying the posterior level of the diencephalon on the right side. Microscopic studies showed that this lesion was a spongioblastoma polare. These observers, in reviewing the literature, cited Fulton and Bailey in the explicit statement that they had seen manic attacks only in cases of tumors affecting the area in the vicinity of the base of the brain, never of neoplasms affecting the hemispheres. Guttmann and Herrmann, as cited by Stern and Dancey, collected 12 cases of circumscribed lesions with manic-depressive psychosis. In all these cases the lesions were localized somewhere between the stalk of the pituitary gland and the anterior margin of the pons. They stated the belief that whenever manic attacks

10. Foerster, O.: Ueber die Bedeutung und Reichweite des Lokalisationsprinzips im Nervensystem, Verhandl. d. deutsch. Gesellsch. f. inn. Med. **46**:117, 1934.

11. Stern, K., and Dancey, T. E.: Glioma of the Diencephalon in a Manic Patient, Am. J. Psychiat. **98**:716 (March) 1942.

were observed, whether transient states of excitement or true psychoses, in association with circumscribed lesions, these lesions were usually localized in the depth of the brain stem or at the base of the brain.

It is difficult to say why the patient whose case has been reported here showed this unusual picture of manic psychosis; one can only speculate on various possibilities. It might be just a coincidence that a manic psychosis appeared in a patient with a brain tumor; this, however, is not probable. In this connection, it is interesting that the manic psychosis disappeared immediately after the first operation and has not recurred up to the time of writing. If the psychosis in this case had nothing to do with the tumor, there probably would have been a recurrence of the mental symptoms after the patient had recovered from the strain of the operation and its immediate consequences. It is also possible that the patient had a potential manic psychosis but had never had a previous attack of a psychotic nature. In this case the tumor might have precipitated the manic attack, or at least brought out the underlying personality structure, as might have occurred with any organic damage of the brain. However, the history taken from the patient and the psychologic studies which were made after the operation—unfortunately, it was not possible to carry out such studies before the operation—do not justify such an assumption. Rather, the psychologic studies showed emotional immaturity which accompanied anxiety on a basically neurotic structure. There is another, rather remote possibility that changes in the brain stem have to do with this affective form of psychosis, in a manner similar to the other cases mentioned in literature. In this case, however, there was no direct involvement of the diencephalon or adjacent areas. An increase of pressure only might have produced physiologic changes there of which we are not aware. As previously mentioned, this possibility is very remote, considering that this patient had only a very moderate increase of intracranial pressure and at no time any symptoms, such as nausea or vomiting, which might indicate such an increase of pressure. There remains the interesting fact that in this case a tumor involved the hemispheres, and there was at the same time a manic form of psychosis. This is in distinct contradiction to previous observations that a brain tumor accompanied with this particular form of psychosis is never located in the hemispheres.

SUMMARY

The case is described of a man aged 29 who had been suffering from generalized seizures of the grand mal type for several years, whose electroencephalograms showed evidence of epilepsy and who had been treated for epilepsy during this time. Finally, there developed the classic picture of a manic psychosis, with all the characteristic symptoms.

The psychosis necessitated hospitalization. A new electroencephalogram brought out a slow focus on the left side, indicating a space-occupying process. This diagnosis was verified by a pneumoencephalogram, showing, however, the tumor on the right side. Operation revealed a parasagittal meningioma occupying chiefly the right side and involving slightly the opposite side. This meningioma was removed in two sessions. There was no further evidence of the manic psychosis after the removal of the tumor.

The literature was reviewed for mention of various mental symptoms, particularly for psychotic pictures associated with brain tumors. Reference is made particularly to the few cases in which a manic psychosis was observed. In most of the cases the brain stem was involved, and in none of them was the tumor a parasagittal meningioma. Speculation is made on the various possibilities which might explain the occurrence of a manic psychosis in this case.

PLEOCYTOSIS AND MENINGEAL SIGNS IN UREMIA

Report on Sixty-Two Cases

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AS A RESULT of our experience with a patient who had three attacks of uremia with as high as 20 lymphocytes per cubic millimeter of spinal fluid during each episode, cell counts were made in 62 consecutive cases of uremia. Patients with a history or findings of syphilis or with any condition that could result in pleocytosis were not included in the series. In the last 30 cases examination was also made for the presence of meningeal signs. In 58 of the 62 cases the uremia was due to renal disorders and in 4 to gastric hemorrhages with prerenal azotemia. The urea content of the blood was calculated from the urea nitrogen determined by the aeration-titration method. The urea value of the cerebrospinal fluid was similarly determined from specimens drawn at the same time as the blood in 29 cases.

An increase in cells in the spinal fluid has been mentioned in isolated instances of uremia by various investigators. Chauffard [1] reported the case of a woman aged 60 with renal disease of three months' duration with uremia. Spinal puncture revealed 50 segmented granulocytes (polymorphonuclear leukocytes) per microscopic field in the fluid on the first day of the illness. Eight days later there were between 6 and 7 cells, and 28 days later, no cells. Lepine [2] found no increase of cells in the spinal fluid in 3 cases of uremia in which such data were given. The meninges were intensely reddened. Lepine stated the belief that the meninges in uremia could be involved in the same manner as the pericardium. Caussade and Willette [3] described a case of uremia with 100

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1. Chauffard, M. A.: Urémie aiguë et polynucléose rachidienne, Semaine méd. **26**:541, 1907.

2. Lepine, R.: Existe-t-il une méningite urémique? Semaine méd. **27**:361, 1907.

3. Caussade and Willette: Urémie convulsive et comateuse; liquide céphalo-rachidien pruriforme, Bull. et mém. Soc. méd. d. hôp. de Paris **25**:199, 1908.

cells per microscopic field; 90 per cent were segmented granulocytes, and 8 per cent were lymphocytes. Two lumbar punctures, performed five and ten days after the first tap, disclosed a clear fluid with no cells. The urea content of the spinal fluid was 40 mg. per hundred cubic centimeters. Mosny and Pinard [4] noted 4 to 18 white cells in the spinal fluid per microscopic field in a patient with uremia four days before death; 88 per cent of the cells were segmented granulocytes, and 11 per cent were lymphocytes and large monocytes. Three days before death there were 15 to 20 cells per field; 52 per cent were lymphocytes, 32 per cent segmented granulocytes and 16 per cent monocytes. The authors attributed the pleocytosis to lead intoxication, but the evidence for the presence of this condition was not convincingly demonstrated. De Massary and Sézary [5] found 40 to 50 white blood cells, chiefly segmented granulocytes, in the spinal fluid of a woman aged 43 with fatal uremia. In Mollard and Froment's [6] eighth case of uremia, numerous red and many altered white cells, almost all segmented granulocytes, were demonstrated in the spinal fluid. In 1 of the cases from other sources referred to by these authors there was an abundance of segmented granulocytes, which diminished after eight days; they were then replaced by lymphocytes. Mestrezat and Anglada [7] reported the case of a woman aged 70 with uremia, hypertension and convulsions. The spinal fluid contained 40 segmented granulocytes per oil immersion field two days before death. The brain and meninges were congested. Nordman [8] described the case of a uremic patient aged 58 with 5 white cells per microscopic field in the spinal fluid at the first lumbar puncture and 1 cell at a later puncture. The meninges were reddened, and there was an old area of softening in the occipital lobe. Augistrou [9] found 25 segmented granulocytes per field in a case of uremia with hemiplegia. Petit [10] described the case of a man aged 43 with uremia. The initial puncture performed on the first day of the illness revealed pleocytosis, with a count of 86 per cent segmented granulocytes, 12 per cent lymph-

4. Mosny, E., and Pinard, M.: Urémie chronique et leucocytose céphalo-rachidienne, Bull. et mém. Soc. d. hôp. de Paris **25**:796, 1908.

5. de Massary and Sézary: Discussion on Mosny and Pinard's case.[4]

6. Mollard, J., and Froment, J.: Urée dans le liquide céphalo-rachidien et urémie nerveuse, J. de physiol. et de path. gén. **11**:263, 1909.

7. Mestrezat, W., and Anglada, J.: Réaction méningée dans un cas d'urémie convulsive et comateuse, Compt. rend. Soc. de biol. **66**:638, 1909.

8. Nordman: Syndromes méningés en cours de l'urémie chronique, Loire méd. **30**:43, 1911.

9. Augistrou, R.: Dissociation albumino-cytologique du liquide céphalo-rachidien, Provence méd. **22**:453, 1911.

10. Petit, P.: Méningite et réactions méningées dans l'urémie, Thèsis de Paris, no. 251, 1912.

ocytes and 2 per cent monocytes. Four days later there was a shift to lymphocytes and monocytes. The total number of cells in the spinal fluid on these two occasions is not stated. Three weeks later a third spinal puncture showed 10 to 12 cells per field, with 70 per cent lymphocytes, 28 per cent monocytes and 2 per cent segmented granulocytes. Trerotoli,[11] in his monograph on nephritis, reported 2 cases of nephritis associated with uremia in which there were occasional segmented granulocytes in the spinal fluid. In 5 cases of nonfatal uremia there were no cells, and in 2 cases of fatal uremia there were "several leukocytes" in the spinal fluid. Alpers,[12] from a study of 98 cases of uremia in the literature, stated that "in 'pure uremia' the pressure is always elevated, the urea content is increased, and by some authors an increase in the sugar and cells has been recorded." He also stated that "the cells are usually normal but may be increased" in cases of associated uremia." In their series of spinal fluid studies, Lyttle and Rosenberg [12a] found 10 or more cells per cubic millimeter in 3 of 10 cases of chronic nephritis with nitrogen retention and edema, 16 and 12 lymphocytes, respectively, in 2 of 5 cases of chronic nephritis with nitrogen retention and no edema and 15 lymphocytes in 1 of 3 cases of acute nephritis with uremia. These investigators concluded that "the presence of uremia has no relation to the cell count." Plaut [13] found counts of 5, 3 and 1 cells per cubic millimeter, respectively, in the spinal fluid in 2 cases of true uremia and in 1 case of pseudouremia. Of Merritt and Fremont-Smith's [14] 56 cases of uremia, 3 had a cell count of 10 or over and 11 a count of over 5 cells. The spinal fluid disclosed no abnormalities in Knutson and Baker's [15] fifth case of uremia. The blood urea nitrogen at the time of the lumbar puncture was 49 mg. per hundred cubic centimeters. Baptista dos Reis and Barini [15a] studied the cell counts in

11. Trerotoli, A.: Il liquido cefalo-rachidiano nelle nefriti, Ann. d. Fac. di med., Perugia **3**:101, 1913.

12. Alpers, B. J.: The Human Cerebrospinal Fluid in General System and Metabolic Diseases as in Nephritis, Diabetes, etc., J. Nerv. & Ment. Dis. **62**:265, 1925.

12a. Lyttle, J. D., and Rosenberg, L.: Cerebrospinal Fluid in Nephritis, Arch. Int. Med. **39**:808 (June) 1927.

13. Plaut, F.: Die diagnostische Bedeutung der "Paralysekurven" der Kolloidreaktionen im Liquor für die nichtsyphilogenen Prozesse des Nervensystems, Ztschr. f. d. g. Neurol. u. Psychiat. **151**:89, 1934.

14. Merritt, H. H. and Fremont-Smith, F.: The Cerebrospinal Fluid, Philadelphia, W. B. Saunders Company, 1938, p. 212.

15. Knutson, G., and Baker, A. B.: The Central Nervous System in Uremia: A Clinicopathologic Study, Arch. Neurol. & Psychiat. **54**:130 (Aug.) 1945.

15a. Baptista dos Reis, J. and Barini, O.: O líqüido cefalorraqueano nas encefalites psicóticas azotêmicas agudas (Marchand), Arq. neuro-psiquiat., São Paulo **6**:241 (Sept.) 1948.

11 cases of psychoses with uremia. In 2 cases with increased counts of 5.6 and 19 cells, respectively, per cubic millimeter, septicemia was a complicating factor.

In our series of 62 cases, the spinal fluid in 16 had 10 or more white cells per cubic millimeter; in 25 cases there were more than 5 cells per cubic millimeter. The highest figure was 250 lymphocytes.

In table 1 are listed the cases with 10 or more cells per cubic millimeter. We do not believe that the pleocytosis is solely due to chemical irritation of the meninges by the increased urea content of the spinal fluid, since we found no consistent relation between the pleocytosis and

TABLE 1.—*Data in Cases of Uremia with 10 or More Cells per Cubic Millimeter of Cerebrospinal Fluid*

Case No.	Cells in Cerebrospinal Fluid/Cu. Mm.	Blood Urea, Mg./100 Cc.
1	13 lymphocytes	195
2	40 lymphocytes	90
3	30 lymphocytes	112
4	26 lymphocytes; 310 erythrocytes	317
5	25 lymphocytes	279
6	60 lymphocytes	207
7	20 erythrocytes; 10 segmented granulocytes (polymorphonuclear leukocytes)	227
8	10 segmented granulocytes	315
9	40 segmented granulocytes	128
10	0	330
	162 segmented granulocytes (15 days later)	261
11	425 noncrenated erythrocytes; 190 leukocytes	407
12	50 lymphocytes	165
13	24 lymphocytes	328
14	250 lymphocytes	463
15	140 lymphocytes	190
16	14 lymphocytes	269

the urea content of the fluid. We had several instances in which the urea content of the spinal fluid was as high as 445 mg. per 100 cubic centimeters with no increase in cells. On the other hand, in 1 case in which the spinal fluid contained 165 mg. of urea per hundred cubic centimeters there were 50 lymphocytes per cubic millimeter. Caussade and Willette [8] stated the opinion that the cells in the spinal fluid in uremia were increased only in the presence of cerebral hemorrhage or thrombosis, which may be subclinical. In our series, there was clinical evidence of a hemiplegia in 1 case, and the autopsy studies of the fatal cases did not disclose hemorrhages or thromboses.

Meningeal irritation, as demonstrated by the presence of nuchal rigidity or the Kernig sign or both, has been described occasionally in cases of uremia. Jaccoud [16] mentioned stiffness of the neck in 3 fatal

16. Jaccoud, S.: Leçons de clinique médicale, Paris, Adrien Delahaye, 1867, p. 737.

cases of uremia which did not show any meningeal lesions. Canac [17] reported a case of a woman aged 24 with meningeal signs. The diagnosis was tuberculous meningitis with pulmonary tuberculosis. However, the only lesions found at autopsy were in the kidneys, with congestion at the apex of one lung. Weiss [18] recorded 2 cases, both of a condition diagnosed as tuberculous meningitis, in which the only lesions found were in the kidneys. Garrod's [19] patient, a boy of 10, had a stiff neck and the Kernig sign. The onset was with hematuria and diminution in urinary output. Garrod stated the opinion that the condition was uremia and that the meningeal irritation was part of the picture. Unfortunately, studies of the spinal fluid were not made on this patient. In the cases of Nordman [8] and Petit [10] meningeal signs were present. Caussade and Willette,[3] Lepine [2] and Mestrezat and Anglada [7] noted the absence of meningeal signs in their cases. In Thévenet and Pehu's [20] case of uremia a Kernig sign was elicited;

TABLE 2.—*Urea Levels in the Blood and Spinal Fluid*

Urea Content, Mg./100 Cc.	Blood, No. of Cases	Spinal Fluid, No. of Cases
Below 150	3	9
Between 150-245	19	16
Between 250-349	33	5
Between 350-449	4	3
Over 450	3	3
Total number of cases	62	29

however, no spinal puncture was done. Shields [21] examined 100 patients, all nonmeningitic, for the Kernig sign. One, a man aged 61 with uremia, had the Kernig sign, which disappeared in eight days.

We tested 30 of our uremic patients for the Kernig sign and nuchal rigidity. Nine of the patients presented both; 1 had only the Kernig sign. Six of the patients had meningeal signs with pleocytosis, with a count of 10 or more cells per cubic millimeter; 4 had meningeal signs without pleocytosis. Four had pleocytosis with a count of 10 or more cells and no meningeal signs; 13 had no meningeal signs and no pleocytosis. Although our results suggest that meningeal signs were

17. Canac: Uremia simulante una meningite tuberculosa, Boll. d. clin. **2**:247, 1885.

18. Weiss, N.: Zur Symptomatologie und Theorie der akuten Urämie, Wien. med. Wchnschr. **31**:89, 1881.

19. Garrod, A. E.: Uraemia or Meningitis? Lancet **1**:835, 1909.

20. Thévenet, J. A., and Pehu, M.: Syndrome cérébrospinal vraisemblablement urémique avec signe de Kernig, Lyon méd. **47**:430, 1901.

21. Shields, W. G., Jr.: Report of One Hundred Cases, All Non-Meningitic, Examined for Kernig's Signs, Am. J. M. Sc. **123**:781, 1912.

found more frequently in patients with pleocytosis with a count of 10 or more cells per cubic millimeter, the series is too small to permit a definite conclusion as to the relation between the presence or absence of meningeal signs and pleocytosis.

The urea levels of the blood and spinal fluid obtained in our series are shown in table 2. The lowest urea value for the blood was 133 mg., and the highest 486 mg., per hundred cubic centimeters. The lowest urea content of the spinal fluid was 140 mg., and the highest 525 mg., per hundred cubic centimeters. Canti [22] stated that the urea content of the spinal fluid, whether it was normal or increased, was approximately the same as that of the blood. In Becher's [23] case 20 the urea value for the spinal fluid was higher than that for the blood. Booij,[24] in a series of 67 patients, found the urea content of the spinal fluids lower than that of the blood in 37, higher in 27 and the same in 3. This investigator considered that the higher urea level of the cerebrospinal fluid was due to a pathologic process resulting in the formation of urea from the parenchyma of the brain. In 6 of our 29 cases the urea value for the cerebrospinal fluid was greater than that for the blood.

The fatal cases in our series confirm the statement of Canti [22] that a cerebrospinal fluid content of urea of 300 mg. or more per hundred cubic centimeters is generally fatal.

CONCLUSIONS

1. In a series of 62 cases of uremia, pleocytosis with a count of 10 or more white cells was found in 16; the highest cell count was 250 lymphocytes.

2. There was no definite relation between the degree of pleocytosis and the urea content of the cerebrospinal fluid.

3. The urea value of the cerebrospinal fluid was higher than that for the blood in 6 of 29 cases studied.

4. Meningeal signs were demonstrated in 10 of 30 cases of uremia.

22. Canti, R. G.: The Urea Content of the Cerebrospinal Fluid, Lancet **1**:344, 1916.

23. Becher, E.: Die Bedeutung des Liquor cerebrospinalis für die Pathogenese der Urämie, München. med. Wchnschr. **73**:146, 1926.

24. Booij, J.: Enkele beschauwingen over het ureumgehalte van den liquor cerebrospinales, Nederl. tijdschr. v. genessk. **84**:2997, 1940.

THE PSYCHIATRIST IN THE GENERAL HOSPITAL

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DETROIT

PSYCHIATRY has moved far from the mere custodial care of the insane. One psychiatrist may have an entirely different type of practice from another. One may devote himself to the care of hospitalized psychotic patients, and another may work with children or adults in the field of mental hygiene. One may "specialize" in the care of mentally defective patients, alcoholic patients, drug addicts or criminals, and another may give intensive psychoanalytic therapy. Again, one may have a sort of "general practice" of psychiatry. The closer his working association with other doctors of medicine, the more likely it is that the psychiatrist's practice will be general.

This paper is a statistical study of the practice of one such psychiatrist during the twelve month period from July 1, 1948 to June 30, 1949. The work was done in a general hospital, which has approximately 600 beds, 30 or more of which are devoted to the care of psychiatric inpatients. The hospital has a full time staff of surgeons, internists and psychiatrists. In addition to the care of inpatients, there is an active outpatient service. The psychiatrists not only serve as consultants, but also treat their own patients, both on an inpatient and an outpatient status.

NUMBER OF PATIENTS CONTACTED

The total number of patients seen by this one psychiatrist was 572 (table 1); of these, 434 (76 per cent) were new, that is, were seen by the psychiatrist for the first time during the current year; 138 (24 per cent) had been seen by him at least once before July 1, 1948. In this series, 371 patients (65 per cent) were classified as having psychoneurotic trends; 88 (15 per cent) had affective disorders, mainly depressions; 61 (11 per cent) had schizophrenia or nonorganic paranoid states; 23 (4 per cent) were alcoholic or addicted to drugs, and 29 (5 per cent) had miscellaneous conditions, chiefly organic disorders with psychiatric symptoms. There were 227 patients who received inpatient therapy; of these, 103 had subsequent outpatient service. One hundred and thirty-two patients were treated only as outpatients during the current year; 183 were seen only in a consultant capacity, and another 30 were referred to other psychiatrists for continuation of therapy (table 2).

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TABLE 1.—*Diagnosis and Results of Treatment of Psychiatric Patients*

	Improved	Sustained	Advised	Unimproved	Referred	Still Under Treatment	Total	Percentage of Total No.
Psychoneurosis								
Inpatient treatment	25	22	0	8	6	3	64	....
Outpatient treatment	39	33	29	19	10	10	140	....
Inpatient consultations	0	0	140	0	9	0	149	....
Situational problems								
Outpatients	1	5	12	..	..	..	18	....
Subtotals and percentages of dispositions, including patients "advised"	65 20%	60 18%	181 54%	27 8%	25 ..	13 (100%	371 ..333)	65%
Excluding patients "advised"	43%	39%	..	18%	..	(100%	..152)	
Affective disorders								
Inpatient treatment	54	9	..	8	1	7	79	
Outpatient treatment	6	2	..	1	..	..	9	....
Subtotals and percentages of dispositions	60 75%	11 14%	.. ..	9 11%	1 ..	7 (100%	88 ...80)	15%
Schizophrenia and paranoid state								
Inpatient treatment	16	10	..	18	..	5	49	
Outpatient treatment	2	5	1	2	2	..	12	
Subtotals and percentages of dispositions excluding patients "advised"	18 34%	15 28%	1 ..	20 38%	2 ..	5 (100%	61 ...53)	11%
Addiction to drugs and alcohol								
Inpatient treatment	5	6	..	6	1	1	19	
Outpatient treatment	..	..	..	2	1	1	4	
Subtotals and percentages of dispositions	5 27%	6 31%	.. ..	8 42%	2 ..	2 (100%	23 ...19)	4%
Miscellaneous conditions (mostly organic)								
Inpatient treatment	9	2	..	11	..	2	24	
Outpatient treatment	1	3	1	..	..	..	5	
Subtotals and percentages of dispositions, excluding patients "advised"	10 38%	5 19%	1 ..	11 42%	.. ..	2 (100%	29 ...26)	5%
Totals and percentages of dispositions, including patients "advised"	158 31%	97 19%	183 36%	75 14%	30 ..	29 (100%	572 ..513)	100%
Excluding those "advised"	48%	29%	..	23%	..	(100%	..330)	

TABLE 2.—*Results According to Type and Place of Treatment*

Patients seen only for advice or referral to other psychiatrists	Advised	Referred	Totals
Inpatient consultations	140	9	149
Outpatient consultations	43	13	56
Referral after some therapy	...	8	8
Subtotals	183 (32%)	30 (5%)	213 (37%)

Inpatient treatment	Improved	Sustained	Unimproved	Still Under Treatment	Totals
No outpatient follow-up	42	32	40	10	124
1 to 3 outpatient visits	62	10	1	6	79
4 to 10 outpatient visits	5	6	10	2	23
More than 10 visits	..	1	..	..	1
Subtotals	109	49	51	18	227 (40%)

Outpatient treatment only during current year	Improved	Improved After Long Previous Treatment	Sustained	Unimproved	Still Under Treatment	Totals
1 to 3 outpatient visits	11	3	32	9	1	56
4 to 10 outpatient visits	19	13	15	15	4	66
More than 10 outpatient visits	1	2	1	..	6	10
Subtotals	31	18	48	24	11	132 (23%)
Totals	..	..	..	..	..	572 (100%)

If one psychiatrist saw 572 patients in one year, he, obviously, gave brief treatment to the many, rather than intensive treatment to the few. The 227 psychiatric inpatients had 5,110 hospital days (average, 23 days per patient), and 1,014 outpatient clinic visits were made, or a total of more than 6,100 "patient contacts" during the year, exclusive of the 213 patients seen for consultation only or for reference to other psychiatrists. Therefore, if the physician devoted 2,000 hours a year to the direct clinical treatment of patients, his average "patient contact" consumed less than twenty minutes. This is, of course, an average figure, and some patient contacts were far more time consuming than that; but it is then obvious that some patients got less of the personal time of the psychiatrist. The aid of junior physicians, particularly in the care of inpatients, is a factor which makes it possible to give adequate care to all patients in these circumstances.

The brevity of the therapy, so far as the personal time given by the psychiatrist is concerned, is further illustrated by the following calculation: If the psychiatrist devoted 2,000 hours a year to clinical work and used 200 of those hours for the 213 patients seen only in a consultant capacity (table 2), the treatment of the remaining 359 patients consumed 1,800 hours. The average period of personal patient-psychiatrist contact, in which were to be accomplished the diagnosis, treatment and final disposition, was therefore five hours.

CONSULTATION SERVICE

If a patient with a mild psychiatric disorder falls first into the hands of an internist or a surgeon, he is likely to be treated by that physician. That is as it should be. But if progress is not satisfactory, psychiatric consultation is requested. The psychiatrist can then either accept the patient for therapy or advise the referring physician how he may carry on. Of 216 such inpatients for whom consultation was requested, the psychiatrist accepted 31 per cent for therapy (52 patients remaining as inpatients under the care of the psychiatrist and 15 patients being accepted for outpatient psychiatric care). The service given by the psychiatrist to the remaining 149 (69 per cent) was in the form of advice to the patient and to the referring physician.

This arrangement is almost ideal in theory, for it keeps the internist actively engaged in the treatment of the bulk of the emotional problems he encounters, without requiring him to care for any particular patient whom he is not equipped to treat. Furthermore, this permits the patient to make his first psychiatric contact as casually and as calmly as he would consult any other medical specialist. If the system does not always work ideally, it is usually because the psychiatrist and the internist are both pressed for time. What if the average time for treating a psychiatric patient was, in this series, "only" five hours? That time may be difficult to find.

USE OF SOMATIC METHODS

Somatic treatments make far less demand on the personal time of the physician than does psychotherapy. The more we psychiatrists can use somatic methods effectively, the more patients we individually can treat, and the closer we come to supplying the demand for psychiatric services. Patients, too, pay more readily for somatic methods. These considerations may be responsible for the fact that somatic methods may sometimes be improperly used. However much we may hope for further advancement in rapid, mechanistic, efficacious treatment, during the year under consideration somatic therapy proved to be the answer to only a small proportion of the problems met by the psychiatrist. Only 110 (20 per cent) of the 572 patients contacted had somatic therapy

TABLE 3.—*Results of Types of Inpatient Treatment*

	Improved	Sustained	Unimproved	Still Under Treatment	Total No.	Percentage of Total Inpatients
Psychotherapy and symptomatic care.	48	33	31	5	117	52%
Percentage of dispositions	43%	29%	28%	(100%..112)		
Somatic therapies						
Electric shock	44	6	15	6	71	
Narcosis	8	5	3	3	19	
Other somatic therapies	9	5	2	4	20	
Subtotal and percentage of dispositions	61	16	20	13	110	48%
	63%	16%	21%	(100%...97)		
Totals and percentage of dispositions	109	49	51	18	227	100%
	52%	24%	24%	(100%..209)		

(table 3). The group treated somatically did constitute 48 per cent of those receiving psychiatric inpatient therapy, that is of the more severely ill patients. In the group of 227 inpatients, somatic treatment resulted in somewhat better rates and degrees of improvement (table 3). It should, of course, be understood that all the patients received psychotherapy, depending on their needs; somatic treatment and psychic treatment supplement each other, rather than being exclusive.

RESULTS OF TREATMENT

Explanation of the terms used in analyzing the value of the psychiatric contact is in order. In the calculation of percentage rates of improvement, 29 patients were excluded because they were still continuing active therapy, and 30 others were excluded because they had been referred to other psychiatrists and the psychiatric contact here recorded could not be considered definitive and final. The referral was necessary at times because the psychiatrist did not have the time available for the

psychotherapy the patient needed, and at other times because it was more practical for the patient from out of town to seek his psychiatric aid nearer home.

The term "advised" refers to the 183 patients (36 per cent) who were seen only in a consultant capacity. It is impossible to determine accurately whether or not the advice given has resulted in improvement, nor is it possible to know what has been the opinion of the referring physician about the value of the advice. However, since the group with which I am associated works together closely, no news about the patient after the psychiatric contact may usually be considered good news. If the referring physician found himself still unable to handle the situation with the advice given, he would ask the psychiatrist to see the patient again or to take over personally the management of the case. If the patient became disgruntled and changed doctors, this information would probably directly or indirectly reach the psychiatrist, in which case the patient would be counted among the "unimproved." The group of "advised" patients is large enough to be significant only with reference to psychoneurosis. In the tables, rates of improvement have been calculated both to include and to exclude the patients advised.

The term "sustained" refers to the numerous psychiatric patients with well defined symptoms who, nevertheless, live a relatively normal life. The person is more unhappy, tenser, more tired, more anxious, more irritable and subject to more somatic dysfunctions than the average; nevertheless, he does "carry on." Symptomatic medication, attention to physical disorders which add to his emotional burden, advice regarding mental and physical hygiene and emotional support are all definite aids to him. Such measures do not modify his underlying personality materially, but they are therapy. Without such treatment by the psychiatrist or by some one else, the person will very likely make more dramatic and more unwise attempts to find peace and comfort—in a new spouse, a new job, a new faith healer, a new operation, a new drug—or he may "decompensate" emotionally, his symptoms becoming so severe that he cannot continue to "carry on."

With reference to the patient whose acute illness was of psychotic or near-psychotic degree, the term "sustained" has the same significance as "social recovery" when used by a state mental hospital. The patient is in the community, making an adjustment at some level, although not necessarily free from symptoms or signs of psychiatric morbidity. With reference to the psychoneurotic patient, the term means that the patient, during the period of observation, is not retreating into any form of psychoneurotic invalidism. Only a longer period of observation than that covered by this study would permit a determination of the proportion of patients "sustained" as of 1949 who improve or become worse as the years pass.

In analyzing the value of psychiatric contact, one must, of course, pay attention to the accepted prognosis of the various disorders. In the affective disorders, one expects about 80 per cent of patients eventually to recover with supportive therapy, regulation of the environment and protection from suicide. Electric convulsion therapy probably does not materially increase the proportion of patients who recover, but it certainly often shortens dramatically the course of the illness. Occasionally it seems to help the patient make a partial recovery, after which supportive psychiatric treatment and the passage of time gradually lead to more complete recovery. In this group, the results for 80 patients are statistically analyzed: sixty (75 per cent) were improved, that is, were well enough to be discharged from regular observation; another 11 (14 per cent) were sustained, that is, were not as well as before the depression began but were "carrying on," with the expectation of further gradual improvement, and 9 (11 per cent) remained unimproved, or improved and relapsed almost immediately (table 1).

Of patients with schizophrenia, it is generally expected that from 30 to 50 per cent who are ill less than a year will have a remission which permits return to the community ("social recovery"). The effect of the shock therapies, again, seems to be primarily that of shortening the duration of the attack. However, in schizophrenia there is some reason to believe that overt schizophrenic behavior and psychotic thinking tend to become fixed, and therefore to interrupt the acute attack as promptly as possible may well serve to make less the susceptibility to future schizoid morbidity. In almost all the cases in this series the disease was of relatively short duration. Of 45 schizophrenic patients and 8 with a paranoid state, 18 (34 per cent) were improved, that is, had a remission of good quality, and 15 (23 per cent) were sustained, that is, had sufficient recompensation in their schizoid processes that they could return to the community at a level of adjustment better than mere custodial care by relatives. This still leaves a significant number, 20 (38 per cent), who were unimproved, often after long and expensive hospital treatment. Schizophrenia is still a tragic disorder, and there is urgent need of much better therapy for it than is now available (table 1).

Neither the group of alcoholic patients and drug addicts nor the group with miscellaneous conditions is large enough to make analytic discussion worth while.

Of the 333 patients statistically considered who exhibited psychoneurotic trends or emotional upsets about situational problems, 181 (54 per cent) were seen only in a consultant capacity. The remaining 152 patients received inpatient or outpatient treatment. Of the latter number, 65 (43 per cent) were considered improved. In this instance, the term "improved" means that the symptoms were definitely less

severe and the patient was thought to have gained some insights which would make his liability to future psychoneurotic decompensation somewhat less. Sixty other patients (39 per cent) were considered "sustained"; that is, they were carrying on in spite of symptoms. It is to be hoped that each of them is learning the rather painful lesson that he must adjust himself to reality, rather than expect reality to take pity on his discomfort and adjust itself to him. Such patients might, without stretching the term too far, be considered "moderately improved," and it is likely that those who do learn the aforementioned painful lesson will gradually be troubled less by their symptoms. Because some of these "sustained" patients will probably slip, it would be overly optimistic to say that in 82 per cent (43 + 39 per cent) the result has been favorable. However, it is justifiable to claim favorable results in about 70 per cent. In only 27 (18 per cent) was the result definitely unfavorable.

Denker [1] reported on 500 patients who were disabled by psychoneurosis for at least three months and treated by general practitioners; 72 per cent of that group had recovered within a two year period, and only 10 per cent were still disabled after five years. It seems that general practitioners have secured as good results as those reported here. Other psychiatrists who have submitted their work to numerical analysis have nothing better to report. Denker cited reports by five psychiatrists, who gave improvement rates from 60 to 83 per cent. He also cited four reports concerning intensive psychoanalytic therapy, and the improvement rates were still very similar— from 50 to 70 per cent. All this leads directly to the interesting thought that perhaps psychoneurosis, like the affective disorders, is usually self limited in its exacerbations.

Other data suggest the same conclusion. For instance, it is commonplace to hear enthusiastic testimonials for patent medicines or for various forms of charlatanism. Use of these unscientific, and sometimes dishonest, measures must therefore often be coincident with subjective improvement, although, we say, certainly not responsible for the improvement. Also, we expect the psychoneurotic patient to tell of other obviously emotional illnesses in the past from which he has "recovered." We mentally reject the reason the patient offers for the illness and for the recovery; we seek in the circumstances surrounding the illness and the recovery the emotional factors which are in our mind "really" responsible. It is as though we accept the fact that psychoneurosis runs an episodic course, recovery being largely unrelated to the "treatment."

1. Denker, P. G.: Results of Treatment of Psychoneurosis by the General Practitioner, New York State J. Med. **46**:2164 (Oct.) 1946.

Yet we rather blandly assume that the treatment we administer not only is responsible for the improvement in the current episode but also will surely prevent further episodes. It is good that we have faith in our methods. But others who treat psychoneuroses are probably just as sincere in their faith in their methods. Whether it be grandmother giving a herb remedy, the chiropractor making an adjustment, the Christian Scientist giving a reading or the psychiatrist giving an interpretation of unconscious material, the faith of the therapeutist in his method is not likely to be shaken when 7 of 10 patients improve coincidentally with the treatment.

The medically trained psychiatrist, of course, knows the principles of scientific method and therefore can, by objectivity and healthy self scrutiny, gradually learn why his treatments generally work and why they sometimes do not. The only thing which has given, and which will preserve, more respect for us as psychiatrists than for the intuitive "healers" is the devotion of our teachers and of each of us to scientific method. Psychiatric literature would be more convincing to other physicians if we followed habitually the same rules they follow when reporting on methods of treatment—the use of a large number of cases and adequate controls.

I shall leave unsettled the question whether the improvement here reported for the psychoneurotic group was more rapid, more lasting or of better quality than might have been obtained by some other physician, be he general practitioner, psychiatrist or psychoanalyst. Different physicians, although all treating patients with conditions correctly diagnosed as psychoneurosis, may still be treating vastly different kinds of persons. It is encouraging to be able to expect some improvement in the majority (say, 50 to 80 per cent) of psychoneurotic patients from relatively simple and common sense methods. The practical consideration for the busy physician is always; "How much time will it take?"

I shall consider that question from the standpoint of the general practitioner and the internist. Of 333 patients with psychoneuroses, the psychiatrist returned 181 (54 per cent) to the care of the internist or of the general practitioner (table 4). This means that he thought the disturbances were mild enough to be materially helped by psychotherapy on the conscious level—face to face discussion of the meaning of symptoms, the role of emotions, the stress of present circumstances and the effect of well remembered past events in molding the present attitudes, habits of thinking, acting and feeling of the patient. The prognosis for this group with milder disorders—somewhat more than half of all the psychoneurotic patients—may be illustrated by a report by

Moss,[2] whose cases were apparently of this type. He stated that from 50 to 66 per cent of the patients he saw four times had significant improvement. Those are the patients, and that is the brief, simple, common sense psychotherapy, with which we psychiatrists want the help of other physicians.

The patients who fail to respond to that therapy are the ones who should come as promptly as possible into the hands of the psychiatrist. Unfortunately, in our present state of knowledge, treatment by the

TABLE 4.—*Treatment of Patients with Psychoneurosis and Situational Problems*

	Improved	Improved After Long Treatment	Sustained	Unimproved	Total	Percentage of Total Patients Handled
Persons treated as inpatients and as outpatients during current year	25	..	22	8	55	....
Percentages	45%	....	40%	15%	100%	....
Persons treated as outpatients only during current year						
1 to 3 visits	7	3	28	5	43	....
4 to 10 visits	14	13	9	14	50	....
More than 10 visits	1	2	1	..	4	....
Subtotals	22	18	38	19	97	....
Percentages	23%	18%	39%	20%	100%	....
Total outpatients treated	47	18	60	27	152	46%
Percentages	31%	12%	39%	18%	100%	
Patients seen only in consultation						
Inpatients					140	
Outpatients					41	
Subtotal					181	54%
Total treated and advised					333	100%
Patients referred to other psychiatrists						
Directly after consultation					19	
After some inpatient treatment					6	
Subtotal					25	
Patients still under active treatment					13	
Total no. of patients with psychoneurosis and situational problems					371	

psychiatrist for these severe illnesses—representing less than half of all the psychoneurotic patients—will not usually be very brief. Of 152 such patients treated by the psychiatrist (table 4), 125 eventually were classified as "improved" or "sustained." This result was obtained in 21 patients (14 per cent) with less than ten outpatient visits per patient. Fifty-seven other patients (38 per cent) were seen only a few times during the current year, but their treatment was not really brief, for almost all had had a more intensive period of therapy, either as inpatients or outpatients, in a previous year. Nineteen of these 57 patients made a rather definite end to their therapy during this year, and they are

2. Moss, R. C.: Office Approach to the Psychoneuroses, M. Clin. North America **31**:1205 (Sept.) 1947.

classified as "improved"; the other 38 are still returning on occasion. They have not been classified as "still under treatment," but, rather, as "sustained," for they do not now need regular and frequent contact with the psychiatrist. They will almost certainly be in a few times during the coming year, but the majority of them, a year or two from now, will probably move into the "improved" group. The 55 patients (36 per cent) who began their therapy with inpatient status during the current year also cannot be considered as having received brief therapy, although, as a rule, they did not require much outpatient follow-up therapy. While in the hospital the psychoneurotic patient regularly requires a larger proportion of the personal time of the psychiatrist than does another type of psychiatric patient. The 19 patients (12 per cent) who remained unimproved after outpatient contact were all persons who gave up therapy after less than ten visits to the psychiatrist.

There is no significant statistical difference in the percentages of favorable outcome (table 4) between the group of psychoneurotic patients who began their therapy with an inpatient status and the group who were treated entirely in an outpatient status during the current year. This observation suggests that hospitalization is indicated for the psychoneurotic patient only if his decompensation is severe, and only until a favorable setting for outpatient therapy has been provided.

SUMMARY AND CONCLUSION

1. One psychiatrist contacted 572 patients in one year. Of these, 64 per cent had psychoneuroses, 15 per cent affective disorders and 11 per cent schizophrenic or paranoid states.

2. Only 20 per cent of the series had somatic types of psychiatric treatment.

3. Thirty-seven per cent were seen only in a consultant capacity; 22 per cent had only inpatient care; 18 per cent had both inpatient and outpatient care, and 23 per cent had only outpatient care during the current year.

4. The stay of the hospitalized patients averaged twenty-three days per patient; the outpatients made an average of 4.3 visits per patient.

5. Of those treated and concluding service during the current year, 48 per cent were considered "improved," 29 per cent as "sustained" and 23 per cent as "unimproved." The term "sustained" implies a gradual movement toward improvement.

6. Of the patients with affective disorders, 75 per cent were "improved" and 14 per cent "sustained." Of patients with schizophrenia or paranoid states, 34 per cent were "improved" and 28 per cent "sustained."

7. For 54 per cent of the psychoneurotic group, the service of the psychiatrist was to give advice to the referring physician. Of those the psychiatrist treated, 43 per cent were "improved" and 39 per cent "sustained."

8. Although the total time the psychiatrist spent face to face with each patient averaged only about five hours, only 14 per cent of the psychoneurotic group were "improved" with less than ten outpatient visits. The remainder of the psychoneurotic patients who were "improved" or "sustained" (68 per cent) had treatment which was more time consuming, either as an inpatient or as an outpatient; some of that therapy was given in a year preceding the period here analyzed.

9. About one-half the psychoneurotic patients had disorders mild enough to be suitable for simple, common sense psychotherapy by the internist or the general practitioner. Up to 70 per cent of this group with milder illnesses can get significant help from as little as four hours of such therapy.

ELECTROENCEPHALOGRAPHIC STUDIES OF THE ENCEPHALOPATHIES

I. Report of a Nonfatal Case of Arsenical "Hemorrhagic Encephalopathy" with Serial EEG Studies

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"HEMORRHAGIC encephalopathy" during arsenical therapy for syphilis was comparatively rare until the advent of rapid treatment methods, several years ago. The incidence of this complication was reviewed by Glaser, Imerman and Imerman,[1] who pointed out that the mortality rate in this complication was 76 per cent. Dorothy Russell,[2] Scheinker [3] and others have noted that the cognomen "hemorrhagic" is really a misnomer and that perivascular necrotic phenomena may be the only notable feature present, rather than the outpouring of red cells.

Engel [4] and his associates, in their studies on delirium, have emphasized the importance of serial electroencephalograms in the evaluation of the degree of clinical and anatomic recovery. In their investigation of a case of acute arsenical encephalopathy they stressed the degree of change in the electroencephalogram, rather than the appearance of any particular wave frequency. Their method was essentially one of quantitative analysis, in which they used their system of frequency analysis. Unlike their case, the one to be reported is an example of severe arsenical encephalopathy with pronounced acute clinical and electroencephalographic changes, which were apparently reversible, as noted in a twelve

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2. Russell, D. S.: Changes in the Central Nervous System Following Arsphenamine Medication, J. Path. & Bact. **45**:357, 1937.

3. Scheinker, I. M.: Genesis of Encephalopathy Due to Arsphenamine (Central Vasoparalysis Due to Arsphenamine), Arch. Path. **37**:91 (Feb.) 1944.

4. Romano, J., and Engel, G. L.: Delirium: I. Electroencephalographic Data, Arch. Neurol. & Psychiat. **51**:356 (April) 1944. Engel, G. L., and Romano, J.: Delirium: II. Reversibility of the Electroencephalogram with Experimental Procedures, ibid. **51**:378 (April) 1944. Engel, G. L., and Rosenbaum, M.: Delirium: III. Electroencephalographic Changes Associated with Acute Alcoholic Intoxication, ibid. **53**:44 (Jan.) 1945. Engel, G. L.; Romano, J., and Goldman, L.: Delirium: IV. Quantitative Electroencephalographic Study of a Case of Acute Arsenical Encephalopathy, ibid. **56**:659 (Dec.) 1946.

month follow-up study. This case of encephalopathy, which followed the second injection of neoarsphenamine, is reported for the following reasons: (1) There was a serial electroencephalographic follow-up study for eight months; (2) the patient recovered from the encephalopathy without notable residual symptoms, and (3) a satisfactory serologic response followed the administration of penicillin.

REPORT OF A CASE

N. B., a white girl aged 16, married, was first seen in the outpatient service on Sept. 1, 1943. She had been married since May 1943 to a soldier, but in July 1943 she had had numerous extramarital contacts. She first noticed a genital ulcer about August 1, and on August 20 her husband had a penile lesion. He reported to his dispensary, where dark field and serologic tests confirmed the diagnosis of syphilis. She appeared at the outpatient service with an ulcer on the labia minora and numerous small ulcerations on the buccal mucous membranes. Dark field examination of the genital and oral lesions revealed active, motile Treponema pallidum. Serologic tests of the blood for syphilis gave positive reactions. However, the patient refused treatment at this hospital and eventually consulted a private physician, who confirmed the diagnosis of syphilis. Six weeks later (October 20) she received the first injection of neoarsphenamine, 0.3 Gm. On October 27, she received 0.4 Gm. of this drug. She had no immediate after-effects from either injection, and in the interval between the two injections she was completely asymptomatic. She awoke on the morning of October 28 feeling "shaky all over" and remained at home the entire day. She had a pronounced startle reaction and tended to be irritable. On the morning of October 29 she was still more tremulous and "jittery." She took her younger sister to a Halloween party at school, and on the way home one of the children called the patient's sister "a Nazi rat." This made the patient hysterical, and she wept and was considerably upset. She continued her way home, and when she saw two men driving an automobile she suddenly screamed, for no apparent reason, became extremely frightened and began running. She went to a friend's home and begged to be taken in because she was afraid some one was after her. The friend quieted her and took her home. Shortly after arrival there she went into the yard; she felt faint. Her legs were weak, and she complained of double vision. In addition, she had several momentary episodes, during which time things would "black out" in front of her. She went to sleep at 8:00 p. m. on October 29 and awoke at 6:00 a. m. the following morning, weak, confused and with difficulty in expressing herself, and showed inability to understand very clearly either the spoken or the written word. She was very irritable and would not eat except when fed, and then only very little. There were generalized muscular twitchings, especially if any noises were made in the room. All that day she remained in bed in a somewhat semistuporous condition, uttering no sounds, although apparently conscious, in that she followed objects but showed no signs of recognition. She was brought to the hospital at 10:00 p. m., October 30, and was able to walk, although she was moderately ataxic. She appeared to be frightened, and any movement by the examining physician or others would cause her to shy away. She either could not or would not talk. If touched, she would jump away in terror. Her eyes were constantly blinking, and there were generalized gross muscular twitchings of all four extremities, the trunk and the face. At 11:00 p. m. she began to have convulsions. These were characterized by tonic-clonic movements beginning in the left upper extremity and then becoming generalized, and lasting from two to thirty minutes. These convulsions continued for four hours, in spite of vigorous therapy.

During this time she received a total of 32 grains (2.08 Gm.) of sodium phenobarbital intravenously together with an additional 4 grains (0.26 Gm.) subcutaneously, 23 cc. of a 2.5 per cent aqueous solution of thiopental (pentothal®) sodium intravenously, 15 cc. of paraldehyde by rectum and, finally, ether by inhalation. The seizures ceased at 3:30 a. m., October 31. The patient rapidly sank into an increasingly severe coma, from which she could not be roused. Through a rather unfortunate error, she received 3 grains (0.195 Gm.) of sodium phenobarbital subcutaneously every three hours until 6:00 a. m., November 1.

On admission, her skin was dry, her breath had a fruity odor and the temperature was 99 F. rectally. The blood pressure was 130 systolic and 80 diastolic. There

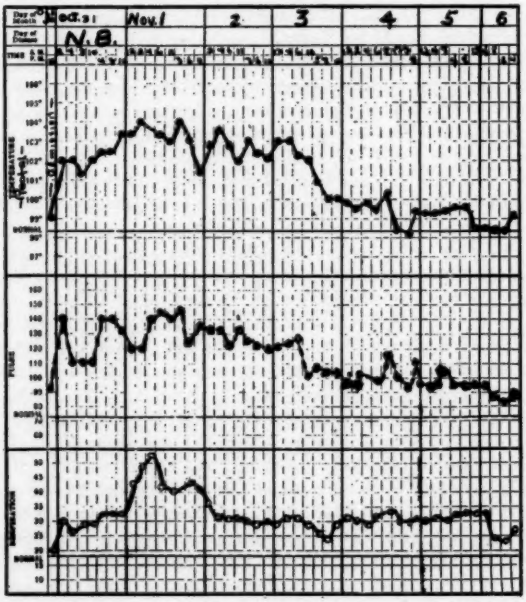

Fig. 1.—Graphic chart of temperature, pulse and respirations.

were numerous scratches over her entire body and a purplish blotching of the skin on both shoulders. Breathing was rapid, and the pulse rate was 140 per minute. Examination of the chest revealed that the breath sounds were harsh. All stretch reflexes were hyperactive, but there were no pathologic reflexes. The white blood cell count was 17,000, with 85 per cent segmented granulocytes. Examination of the urine revealed a 4 plus reaction for acetone and the presence of albumin, and the specific gravity was 1.039. She was treated for acidosis by fluids administered intravenously, and within the next twenty-four hours the urine returned to normal. By 2:00 a. m. of October 31, the temperature had risen to 102 F., and it appeared that death was imminent.

On November 1 her temperature had risen to a maximum of 104 F. (fig. 1); the respiration rate was 50 per minute; coma had deepened, and there was tubular breathing in the bases of both lungs. Roentgenograms revealed a mottled density

in the lower portion of the right lung field, which was thought to be consistent with pneumonia. Sodium sulfadiazine was administered intravenously in an initial dose of 5 Gm. and then continued, 2.5 Gm. being given every eight hours. Examination showed conjugate deviation of the head and eyes to the right. Any attempt to flex the head or turn it to the left caused her to open her eyes widely and mumble. The neck was moderately stiff, and there was a Kernig sign bilaterally. Respirations were Cheyne-Stokes in character. The face was flushed. The pupils were equal and reacted briskly to flashlight. The optic disks were normal, but there was moderate engorgement of the retinal veins. There was definite weakness of the left side of the face of a supranuclear type. To painful stimuli she moved only the right upper and lower extremities. There was an alternating tonic-plastic type of rigidity in both upper extremities. All deep reflexes were absent, and the plantar reflexes were definitely flexor.

The patient was given fluids intravenously (isotonic sodium chloride solution and 5 per cent dextrose) plus 1 Gm. of sodium thiosulfate intravenously every four hours. In addition, 1 cc. of a 1:1,000 solution of epinephrine hydrochloride was administered every four hours for three doses and then continued in one-half this dose at the same interval for twenty-two doses.

TABLE 1.—*Cerebrospinal Fluid Studies**

Date	Appearance	Initial Pressure (Mm. of Water)	Cells	Globulin	Total Protein (Mg./100 Cc. CSF)	Colloidal Gold Curve	Kline Diagnostic Test	Kline Exclusion Test	Kolmer	
									0.5 Cc.	1.0 Cc.
10/31/43	Water	300	3 lymphocytes	4+	274	5555444333	4	4	4	4
11/ 1/43	Water	200	11 lymphocytes	4+	176	3332222211	4	4	4	4
11/15/43	Water	140	5 lymphocytes	—	43	0000000000	—	—	—	—
11/18/43	Water	150	None	—	50	0000000000	—	—	—	—

* Note the elevation of pressure and total protein and the positive reactions to the serologic tests during the acute illness. Note, too, the return of the spinal fluid to normal after recovery by November 15, without the use of specific drugs.

On November 2, the patient was still comatose; the temperature ranged from 102 to 103.5 F., and the nuchal rigidity had disappeared. Resistance to passive manipulation of all four extremities was now normal. All stretch reflexes were hyperactive. The patient began to cough and expectorated much frothy sputum, which showed type III pneumococci. Roentgenograms of the chest now revealed diffuse increase in density throughout the entire right lung field and the left hilus. On November 3 the patient began to rouse with only minimal stimuli and, although unable to talk, carried out a few simple commands. She regained consciousness on November 4 but was disoriented for time, place and person and showed obvious gross memory defects. By November 7 she was much clearer mentally and was able to recognize people. Her lungs showed signs of resolution, so that by November 16 roentgenograms of the chest were normal and the roentgenologist expressed the belief that the process previously described as pneumonic was probably on the basis of a severe pulmonary edema. The temperature returned to normal by November 6, at which time administration of sulfadiazine was discontinued and she remained afebrile. Neurologic examination on November 8 revealed a normal status. By November 16 the patient was able to get out of bed and was asymptomatic. There was generalized hyperreflexia with a bilateral Hoffmann sign. She talked coherently, was rational and was able to describe the events of her present illness up to 8:00 p. m. on October 29 and to piece in some events from the night of November 2.

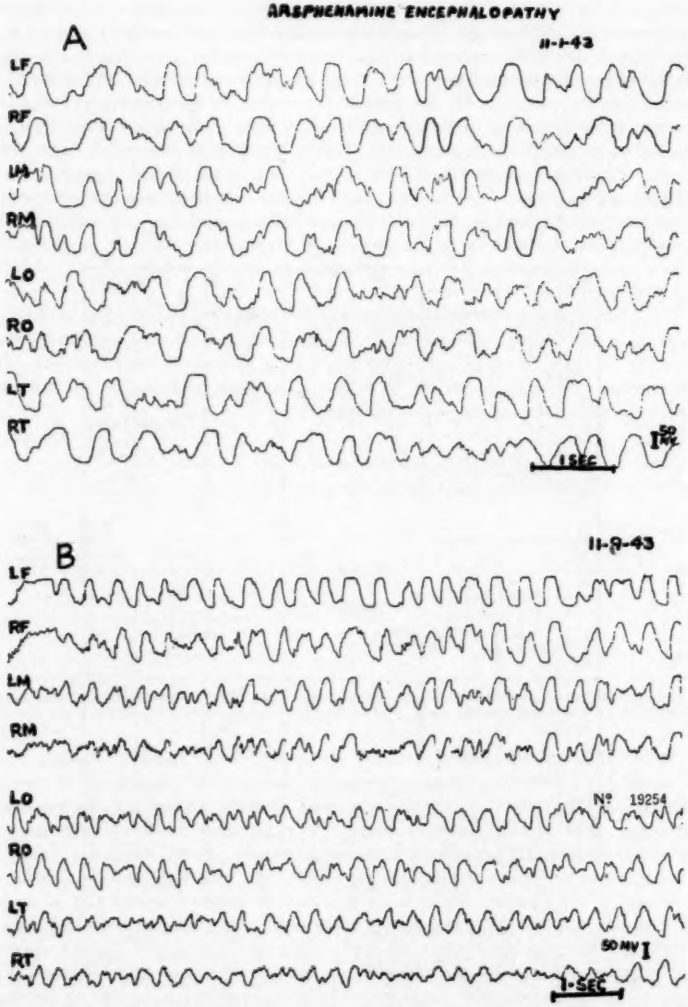

Fig. 2.—Serial electroencephalograms: (1) large high voltage slow waves throughout all areas on November 1, when the patient was comatose (*A*); (2) persistence of slow activity on November 9, although the patient had been conscious four days (*B*); (3) gradual disappearance of the slow waves (*C, D, E, F* and *G*) with an essentially normal electroencephalogram on Jan. 19, 1944 (*H*); (4) appearance of focal slow wave and slow spike discharges on November 16, in the right occipitotemporal region (*C*), prior to onset of focal motor and sensory seizures; (5) subsequent positive or diphasic spike discharges in the right temporal region (*F, G, H, I*); (6) appearance of fast activity on Feb. 23, 1944 (*J*) and its persistence (*K*).

LF indicates tracing from the left frontal region; *LM*, from the left parietal; *LO*, from the left occipital; *LT*, from the left temporal, and *R*, from homologous areas on the right side.

A spinal puncture performed shortly after her admission, on October 31 (table 1), showed an initial pressure of 300 mm. of water. The fluid contained 3 lymphocytes per cubic millimeter, with a total protein of 274 mg. per hundred cubic centi-

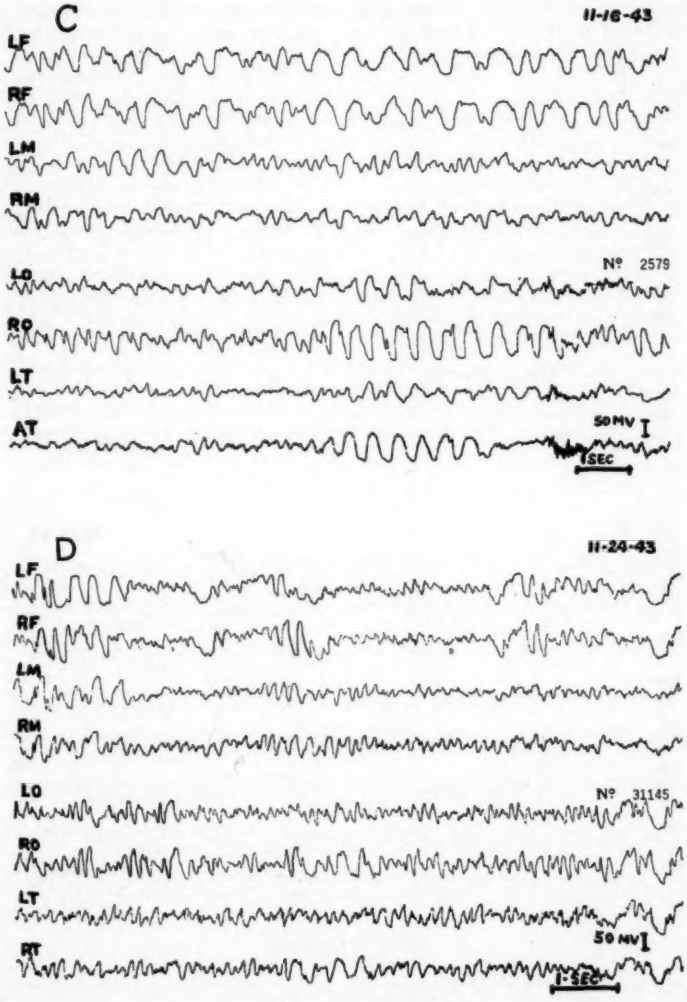

Figure 2 continued

meters of spinal fluid, strongly positive reactions in the Kolmer and Kline tests and a first zone type of colloidal gold curve. The spinal fluid picture was essentially the same on November 1, but by November 15 it had returned to normal (table 1).

Inquiry into the patient's past history revealed that she had always been a behavior problem. She had made out poorly in school, completing only the sixth grade, and had left school to go to work. She was very much of a flirt and was the talk of the neighborhood. She was known for her coyness and naïveté. Although physically well matured, she had been considered emotionally and mentally very immature. On her recovery from the severe encephalopathy, she presented a problem

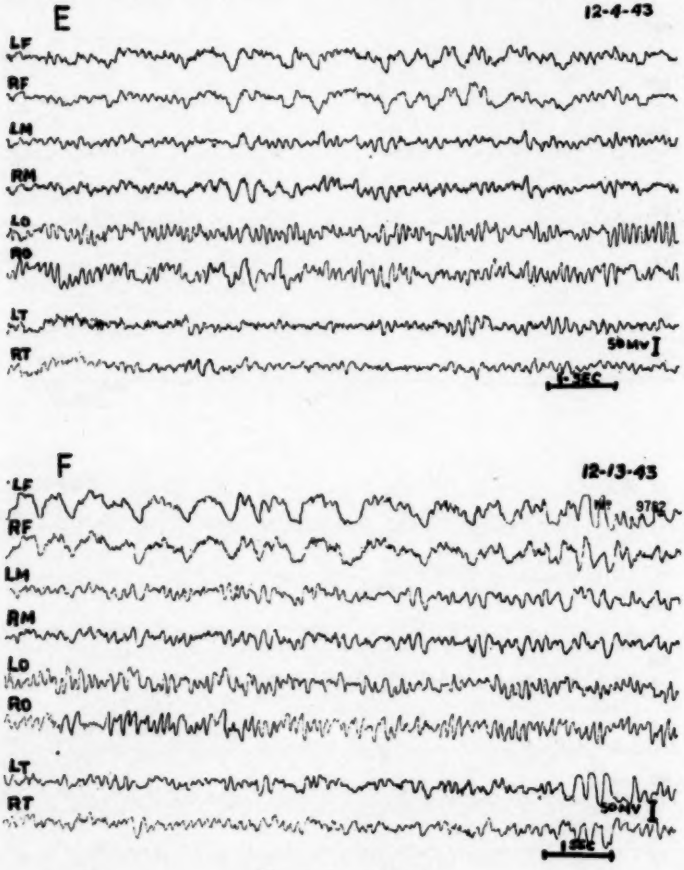

Figure 2 continued

in the ward in her lack of cooperation and her infantile behavior. However, her parents and husband verified the impression that this presented no change over her previous behavior. She had an intelligence quotient of 90 on December 1 and subsequently, a value which corresponded to her preillness level.

About December 5 the patient began to have clonic convulsions, limited to the left upper extremity; these occurred every few days and lasted about one hour. The range of movements was small. They were not associated with any disturbance

in consciousness. In addition, she had sensory episodes during which she experienced a vague sort of numbness involving the left half of the body, beginning in the thumb of the left hand and spreading up the extremity and then down the trunk and the left lower extremity. During these attacks she had blotting out of the left half of the fields of vision. The sensory attacks were preceded by a sensation of

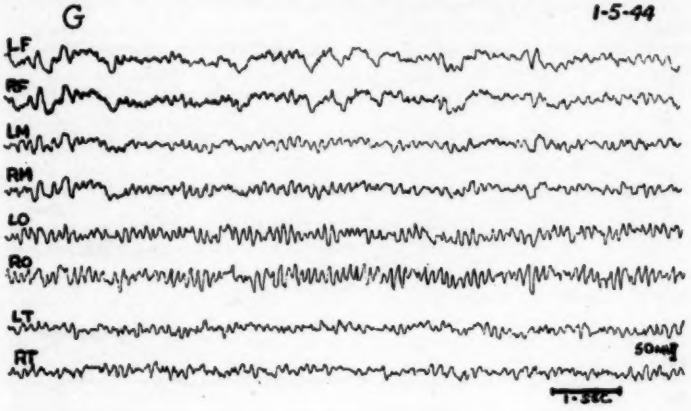

Figure 2 continued

light-headedness. Examination of the patient during the sensory convulsions revealed left homonymous hemianopsia and left hemihypesthesia to all forms of sensation, as well as left hyperreflexia. These episodes gradually decreased in frequency and severity, so that by Jan. 15 1944 they had ceased.

Specimens of blood were subjected to a battery of six serologic tests on Nov. 17, 1943. All tests gave strongly positive reactions (table 2). On November 24 penicillin therapy was started. From November 24 to November 29 she received 30,000

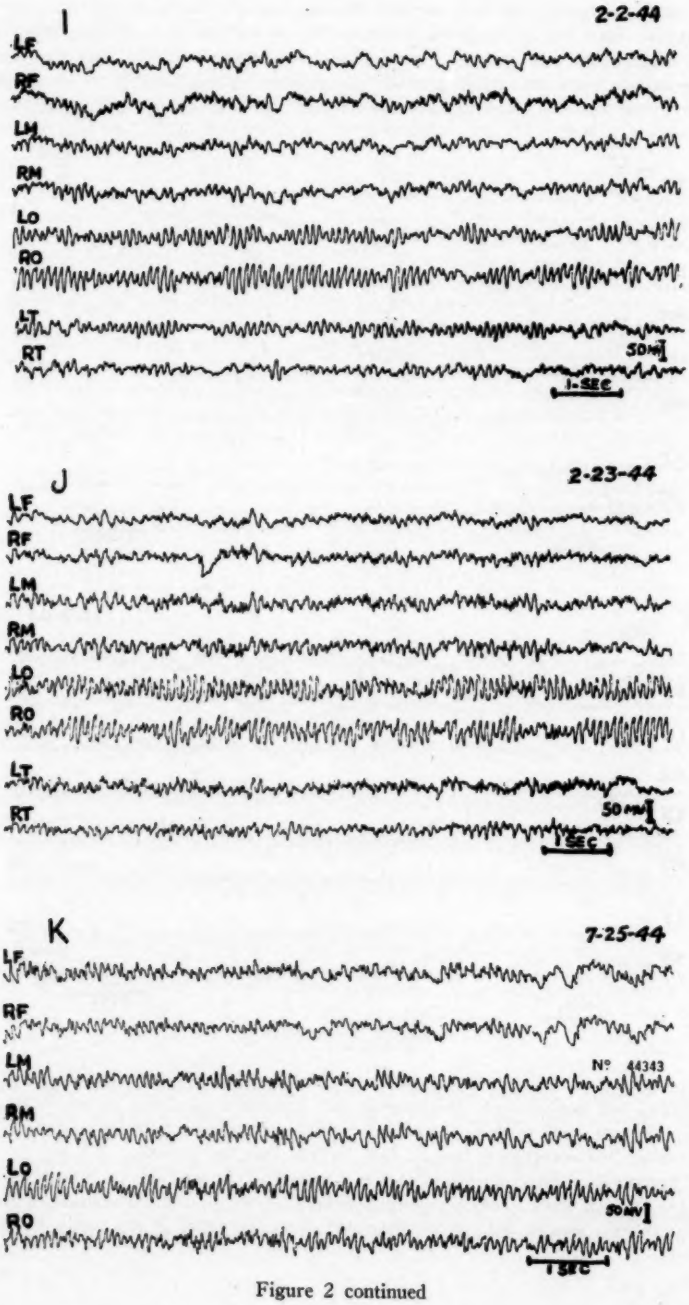

Figure 2 continued

units of crystalline penicillin every three hours, and from November 30 to December 8, 15,000 units every three hours, making a total dose of 2,520,000 units. Another course of penicillin was given from December 13 through December 20, 1943 (25,000 units every three hours) and from December 21 through December 26 (15,000 units every three hours). The combined total dose of penicillin given intramuscularly was 4,800,000 units. Daily serologic studies of the blood were made (table 2). By April 22, 1944 all blood tests gave essentially negative reactions.

The patient was discharged from the hospital on Dec. 29, 1943. She was seen from time to time in the clinic. On July 25, 1944 she reported that she had been feeling well, except for an occasional attack of numbness in her left extremities (she had discontinued the antiepileptic drug). The pictures of the blood and spinal fluid at this time were entirely normal.

Of special interest were the electroencephalographic findings (fig. 2). The first electroencephalogram was made on November 1, at which time the patient was

TABLE 2.—*Reactions in Serologic Tests of the Blood**

Date	Kline Diagnostic	Kline Exclusion	Boerner-Jones-Lukens	Mazzini	Kahn	Kolmer
11/17/43	4	4	4	4	4, 4, 4	4
11/24/43	3	4	4	4	4, 4, 4	4
11/29/43	3	4	2	4	2, 4, 4	4
12/ 3/43	2	4	2	4	1, 3, 3	4
12/ 6/43	2	4	2	4	1, 3, 3	4
12/28/43	2	4	2	3	−, ±, 2	—
1/ 5/44	2	4	2	3	−, ±, 1	—
2/ 4/44	±	3	1	2	—	—
3/15/44	—	1	—	1	—	—
4/22/44	—	±	—	—	—	—
6/28/44	—	±	—	—	—	—
7/25/44	—	±	—	—	—	—

* A battery of six tests were made daily during penicillin therapy, which was initiated on Nov. 24, 1943. Representative reports are given. Penicillin therapy was discontinued on December 26, after a total dose of 4,800,000 units had been administered.

comatose, and revealed a typical stupor record with large high voltage 1 to 3 per second waves. By November 9 the patient had become completely conscious and rational, and at this time the electroencephalogram still showed diffuse slow activity. On November 16 it was noted that the delta waves were disappearing but were especially prominent on the right side in the occipitotemporal region. The tracing from this region assumed a pattern characterized by high voltage, 2 to 3 per second, slow wave and slow spike discharges. This was of interest in view of the fact that the patient had had focal convulsions involving the left side and there subsequently developed jacksonian sensory and motor convulsions on this side, associated with visual field defects on the left side. By November 24 the slow activity was even less conspicuous, but the localization in the right occipitotemporal region was still notable, in the form of positive or diphasic spikes. On Jan. 19, 1944 the electroencephalogram was considered normal for the first time. Subsequently, high voltage fast activity was present diffusely throughout the record.

COMMENT AND SUMMARY

A case of severe arsenical "encephalitis" with recovery is recorded. The electroencephalographic findings are particularly stressed. The

nonspecific response of the brain from an electroencephalographic standpoint is the appearance of delta (slow wave) activity.[5] This is true regardless of whether the injury is physical, traumatic, neoplastic, infectious, degenerative or toxic. The severer the injury, the more prominent is the slow activity. The latter usually disappears within three months in the case of a nonprogressive lesion. In the case of a dural-cortical penetrating wound focal epileptogenic discharges appear at the end of this time in approximately 40 per cent of such injuries.[6] These focal discharges usually do not appear until the nonspecific delta waves have been dissipated. Hence, by the use of serial (repeated) electroencephalograms one can receive auxiliary aid in following the course of any disease affecting the cerebral hemispheres. The electroencephalographic changes usually precede, and can indicate, the clinical course. Furthermore, it is possible to predict the appearance of complications, e. g., focal accumulations of blood or pus, or the occurrence of convulsive phenomena.

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5. Roseman, E.: Electroencephalography of Gunshot Wounds of the Brain, in Surgeon General's History of the War: Head Injuries, to be published.

6. Roseman, E., and Woodhall, B.: Electroencephalogram in War Wounds of the Brain, with Particular Reference to Post-Traumatic Epilepsy, A. Research Nerv. & Ment. Dis., Proc. (1944) **25**:200-219, 1946.

News and Comment

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY, INC.

The following candidates were certified at a meeting of the Board in San Francisco, June 23 and 24, 1950.

Psychiatry.—John Richard Adams, Topeka, Kan.; Henry F. Albronda, San Francisco; Howard G. Aronson, Chicago; William M. Asher, Beverly Hills, Calif; Harold Balikov, Chicago; Warren Jackson Barker, Chicago; Maurice J. Barry Jr., Indianapolis; Morton E. Bassan, Seattle; Reginald V. Berry, Oakland, Calif.; Francis Sterlen Bobbitt, Seattle; *Wade Hampton Boswell, Bethesda, Md.; Lazard Samuel Brener, Houston, Texas; Alfred Bronner, Lyons, N. J.; Bernard Brownfield, Palo Alto, Calif.; E. Ivan Bruce Jr., Galesvton, Texas; Leslie Caplan, Minneapolis; Pasquale A. Carone, Brooklyn; Iverson Clark Case Jr., Little Rock, Ark.; Norman Chivers, Cincinnati; William Gideon Closson Jr., San Jose, Calif.; Jess Victor Cohn, Indianapolis; Kenneth Mark Colby, San Francisco; Robert W. Cranston, Minneapolis; Edward C. Dale, Detroit; Harold E. Day, Camarillo, Calif.; August J. Dian, Gary, Ind.; Jackson C. Dillon, Fresno, Calif.; Maurice Dunn, Gulfport, Miss.; Allen J. Enelow, Topeka, Kan.; Marion Monroe Estes, Augusta, Ga.; Fred Feldman, Los Angeles; Thomas L. Fentress, Chicago; Stephen Fleck, Seattle; Louis H. Forman, Kansas City; Merritt W. Foster Jr., Richmond, Va.; Frederick W. Frank, San Francisco; John G. Freeman, Rochester, Minn.; Leslie Sherwood Freeman, Lyons, N. J.; Arthur W. Freidinger, Seattle; Seymour Warren Friedman, Topeka, Kan.; Charles O. Furniss, Topeka, Kan.; Wray R. Gardner, Denver; Lucio Ernest Gatto, Philadelphia; Otto Luke Gericke, Patton, Calif.; Israel Glick, Pittsburgh; Herbert Y. Glicksman, Chicago; Eugene G. Goforth, Seattle; Walter J. Grant, Little Rock, Ark.; John A. Grimshaw, Topeka, Kan.; Kalman Gyarfas, Chicago; Henry Lee Hall, New York; Martin H. Halvorsen, Elgin, Ill.; Eugene A. Hargrove, Philadelphia; G. Leonard Harrington II, Topeka; Paul Henry Harwood Jr., New Haven; James E. Hayden, Washington, D. C.; Roger C. Hendricks, Seattle; Robert Gormely Houlihan, APO #407, c/o Postmaster, New York; Wallace B. Hussong, Camden, N. J.; William C. Jenkins, Denver; Oliver B. Jensen, Livermore, Calif.; Blocker Howe Joslin, Minneapolis; Paul M. Kersten, Topeka, Kan.; Charles Kligerman, Chicago; Michael T. Koenig, Camarillo, Calif.; Robert H. Koff, Chicago; Carl J. Kornreich, New York; Edward H. Kowert, St. Louis; Robert Gerhardt Kuehnert, Chicago; Anna M. Kulka, Los Angeles; Jerome M. Kummer, Santa Monica, Calif.; Harry Clayton Leavitt, Steilacoom, Wash.; Seymour Leshin, Long Beach, Calif.; Montie Magree, Long Beach, Calif.; Charles Adley Mangham, Cincinnati; *Lester H. Margolis, San Francisco; I. Arthur Marshall, Topeka, Kan.; Robert B. McElroy, Waco, Texas; Ladislas Joseph Meduna, Chicago; Ralph H. Meng, Rochester, Mich.; Frank F. Merker, Topeka, Kan.; Eugene Meyer, Baltimore; *Francis J. Millen, Milwaukee; Horace G. Miller, Salem, Ore.; Benjamin Moorstein, Akron, Ohio; Willard Barnes Morell, Imola, Calif.; Robert Stephen Mowry, Palo Alto, Calif.; Robert C. Murphy Jr., Tacoma, Wash.; Charles Pilgrim Neumann, White Plains, N. Y.; Francis Carter Newson, Topeka, Kan.; Joseph Knight Orr, Los Angeles; Maurice Pachter, Canandaigua, N. Y.; Aaron Paley, Topeka, Kan.; Donald Scott Patterson, Santa Barbara, Calif.; Lloyd Clifford Patterson, Berkeley, Calif.; George Alvin Peabody, White Plains, N. Y.;

Robert M. Phillips, Menlo Park, Calif.; Saxton Pope, Berkeley, Calif.; Reese H. Potter, St. Louis; *John Marion Radzinski, Chicago; Bernard Rattner, Chicago; Leonard P. Ristine, Topeka, Kan.; Maurice J. Rosenthal, Chicago; Sidney L. Sands, Des Moines, Iowa; Jerome L. Saperstein, Beverly Hills, Calif.; Mary Alice Sarvis, Berkeley, Calif.; Werner F. Schmidt, Detroit; Robert Richard Schopbach, Clifton Springs, N. Y.; Quinton D. Schubmehl, Clifton Springs, N. Y.; Dwight William Schuster, Indianapolis; Abraham Schwartz, West Los Angeles, Calif.; Philip Franz Durnam Seitz, Indianapolis; Stanton L. Sheimo, San Francisco; Robert John Shoemaker, Pittsburgh; Alec Skolnick, San Mateo, Calif.; LaVern C. Strough, Omaha; Edward L. Suarez-Murias, Baltimore; David C. Summers, Putnam Valley, N. Y.; John Everett Talley, Waco, Texas; Charles Fleming Taylor, Lebanon, Pa.; Fred W. Tempey Jr., Livermore, Calif.; John Wix Thomas II, Berkeley, Calif.; John Crozier Todd, Chicago; George J. Wayne, Los Angeles; Franz W. Wasserman, Oakland, Calif.; Edward Michael Weinshel, San Francisco; James S. Whedbee Jr., Denver; John D. Whitehouse, Pontiac, Mich.; James G. Whitney, Berkeley, Calif.; Joseph Zinkin, Ellis Island, N. Y.; Robert Michael Zirpoli, Chicago.

Neurology.—Wilford Armond Brooksby, Eugene, Ore.; Nathan Emerson Carl, Los Angeles; Thomas W. Farmer, Dallas, Texas; William S. Fields, Houston, Texas; David A. Freedman, New Orleans; Hugh William Garol, San Francisco; Julius Hoffman, Topeka, Kan.; *Roy Sears Hubbs, Palo Alto, Calif.; Lloyd Francis Jenk, Neenah, Wis.; Arnold H. Kambly Jr., Ann Arbor, Mich.; Seymour L. Pollack, Chicago; Clark T. Randt, New York; Bernard S. Schaeffer, Milwaukee; Robert P. Sedgwick, San Francisco; Wayland A. Stephenson, Hines, Ill.; Frederick D. Stern, New York; *Harold A. Stevens, Washington, D. C.; William John Wedell, San Francisco; V. Richard Zarling, Minneapolis.

At its most recent meeting the American Board of Psychiatry and Neurology, Inc., decided that the next examination conducted by the Board would be held in New York city on Dec. 18 and 19, 1950. The number of candidates to be accepted for this examination must be limited to 300. Applications for this examination should be received in the secretary's office before Sept. 1, 1950.

* Denotes Complementary Certification.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Anatomy and Embryology

METACHROMATIC BODIES IN THE BRAIN. MARION C. SMITH, J. Neurol., Neurosurg. & Psychiat. **12**:100 (May) 1949.

The finding of metachromatic bodies, or "mucocytes," within the white matter of the brain in a variety of disorders has led Smith to review the various theories of their origin. The two opposing views are (1) that the "mucocytes" originate from degeneration of either the oliogodendroglia or myelin sheaths, and (2) that they represent artefacts. By various methods of fixation, the author tried to produce these changes but found that they occurred consistently only in certain affected brains. Normal brains contained some degenerative substances which stained similarly, but these were not consistently present. The author concludes that, in his opinion, these bodies originate from mucoid degeneration of the oligodendroglia, myelin or ground substances of the white matter. They are not artefacts of fixation, but, in order that they may be brought out more clearly, the tissue must be treated with absolute alcohol from one to forty-eight hours. They are definitely associated with such neurologic disorders as Huntington's chorea, Schilder's disease (progressive subcortical encephalopathy) and "grass sickness" of horses.

N. MALAMUD, San Francisco.

Physiology and Biochemistry

A COMPARATIVE STUDY OF THE EFFECTS OF OXYGEN LACK ON PERIPHERAL NERVE. ERNEST B. WRIGHT, Am. J. Physiol. **147**:78 (Sept.) 1946.

Wright studied the effects of lack of oxygen on the peripheral nerves of crustaceans, frogs and mammals to determine whether or not an inverse relation exists between the rate of oxygen uptake and the survival time during anoxia. It was found that nerves with low rates of oxygen uptake had long survival times, whereas nerves with high rates of oxygen uptake had shorter survival times. The product of survival time and oxygen uptake is a constant for the species. The survival time varies inversely, and the oxygen uptake directly, with the temperature. Near the cut end of the nerve the survival time is shorter and the oxygen uptake higher than in the intact portion.

FORSTER, Philadelphia.

APPARENT CURARE EFFECT OF SUBSTANCES THAT DECREASE ACETYLCHOLINE SYNTHESIS. CLARA TORDA and HAROLD G. WOLFF, Am. J. Physiol. **147**:384 (Oct.) 1946.

Torda and Wolff studied the effects of various compounds on the response of the gastrocnemius muscle of the frog to indirect stimulation. Uric acid, pyrrole, alloxan, methyl guanidine, vitamin K, ammonia, hydroquinone, α-naphthol, β-naphthol and glyceraldehyde decreased the response of striated muscle to indirect simulation but did not decrease the response of excised striated muscle to acetylcholine. Serum collected from the working arm of human subjects also decreased the response of striated muscle in indirect stimulation and decreased the synthesis of acetylcholine without decreasing the response of excised muscle to acetylcholine.

Torda and Wolff suggest that an apparent curare-like effect may be exerted by substances acting not on some structure or process within the muscle, but on the nerve tissue.

FORSTER, Philadelphia.

EFFECT OF CYANIDE ON THE CONCENTRATION OF LACTATE AND PHOSPHATES IN BRAIN. N. S. OLSEN and J. R. KLEIN, J. Biol. Chem. **167**:739, 1947.

The toxic effect of the cyanide ion on brain in vivo, and other biologic systems, is attributable mainly to its combination with the oxidized form of cytochrome oxidase and consequent interference with oxygen utilization. From this it would follow that the effects of cyanide are essentially similar to those produced by hypoxia. This hypothesis is supported by the reports that hypoxia and cyanide produce an increase in concentration of lactate and a decrease in concentration of phosphocreatine and adenosine polyphosphates in brain in vivo. However, the extent to which the changes following administration of cyanide may be attributable to hypoxia induced by effects on the heart and respiration is uncertain. In the present investigation, the effect of intravenous injection of cyanide on the concentration of lactate and certain organic phosphates in the brain was studied in paralyzed cats maintained with constant artificial respiration. An attempt was made to determine whether direct action of cyanide on the brain could account for the changes observed. The concentration of lactic acid in the brain increases after intravenous administration of subconvulsant, convulsant and fatal doses of cyanide. After administration of the two last-mentioned amounts the concentration of phosphocreatine decreases. The changes evoked by the convulsant, and presumably by the subconvulsant, dose are reversible. The data obtained indicate that the concentration of cyanide in the brain was about 10^{-5} molar thirty seconds after injection. This concentration was maintained for about thirty minutes, after which it fell to about 10^{-6} molar. The concentrations of cyanide in the brain in vivo are adequate to account for the increases in brain lactate that follow administration of cyanide. Since the level of cyanide in the brain was also comparable to that at which oxygen uptake begins to decrease in vitro, and since maintenance of high energy phosphate bonds depends on oxidation, it may be inferred that the oxygen uptake of the brain in vivo was depressed and that the decrease in phosphocreatine was consequent on this depression.

PAGE, Cleveland.

DETERMINATION OF FREE AMINO ACIDS IN RAT TISSUES. P. E. SCHURR, H. T. THOMPSON, I. M. HENDERSON, J. N. WILLIAMS JR. and C. A. ELVEHJEM, J. Biol. Chem. **182**:39, 1950.

The authors report on the free amino acid content of tungstic acid extracts as determined by microbiologic assay of male adult albino rats. Twelve amino acids were so estimated. In nonfasting animals the total content of the brain was 268.5 micrograms per gram, whereas in fasting animals it was 302.5 micrograms.

PAGE, Cleveland.

INFLUENCE OF CHILLING AND EXERCISES ON FREE AMINO ACID CONCENTRATIONS IN RAT TISSUES. J. N. WILLIAMS JR., P. E. SCHURR and C. A. ELVEHJEM, J. Biol. Chem. **182**:55, 1950.

The free amino acid concentration of brain was less affected by chilling and exercise than the amino acid content of other tissues. The most notable change

occurred in the concentration of histidine and arginine, which decreased during exercise. Leucine and valine increased during exercise in all tissues studied. Otherwise, no consistent changes were observed.

PAGE, Cleveland.

EFFECT OF NUTRITIONAL DEFICIENCIES ON DEVELOPMENT OF NEUTRALIZING ANTIBODIES AND ASSOCIATED CHANGES IN CEREBRAL RESISTANCE AGAINST VIRUS OF WESTERN EQUINE ENCEPHALOMYELITIES. I. RUCHMAN, J. Immunol. **53**:51 (May) 1946.

Ruchman studied the influence of underfeeding, deficiency of the whole vitamin B complex, thiamine deficiency, riboflavin deficiency, carbohydrate deficiency and protein deficiency with respect to the development of immunity in mice vaccinated with western equine encephalomyelitis mouse brain virus treated with dilute solution of formaldehyde U. S. P. Underfed mice developed considerable immunity, but not to the same extent as did those on an adequate diet. The well nourished vaccinated mice resisted between one hundred and two hundred times as much virus injected intracerebrally as did the underfed animals. The test for neutralizing antibodies showed that the well nourished animals neutralized between ten and one hundred times as much virus as did the starved mice. The serum of the adequately nourished animals could be diluted between three and eight times as much as that of the undernourished mice and still neutralize the effects of a constant amount of virus. Removal of the whole vitamin B complex from the synthetic diet yielded equivocal results in mice, but a decreased ability on the part of vitamin B–deficient animals to produce antibodies appeared possible. In 1 case a vitamin B–deficient animal acquired a neutralization index which was one-fifteenth that of the control animals. Thiamine or riboflavin deficiency had no effect either on the production of neutralizing antibodies or on the development of cerebral resistance. Protein or carbohydrate deficiency did not cause a decided failure on the part of deficient animals to acquire immunity, but there was a quantitative difference. The cerebral immunity was about tenfold as great in the well nourished as in the deficiently fed mice.

J. A. M. A.

STUDIES ON NEUROMUSCULAR DYSFUNCTION: VII. USE OF CURARE TO DIFFERENTIATE MUSCLE SPASM FROM ORGANIC CHANGES IN LIMITATION OF PASSIVE MOTION AT JOINTS. C. W. JONES, C. B. LECOMPTE and H. KABAT, South. M. J. **39**:799 (Oct.) 1946.

Jones and his associates experimented with curare in the differentiation of organic and functional factors in limitation of passive motion at joints. Seventeen patients showing limitation of passive motion at joints were given curare intravenously in the form of intocostrin® (purified chondodendrontomentosum extract). Each patient received morphine sulfate ⅛ grain (8 mg.) and atropine sulfate 1/200 grain (0.3 mg.) subcutaneously thirty minutes before the administration of curare. Intocostrin® was administered in the operating room by a trained anesthetist, with tracheal tube, respirator and neostigmine close at hand to counteract the curare effect. The intocostrin® was injected slowly into the antecubital vein. Each patient was given the amount of curare that rendered him unable to lift his head from the table and produced weakness of the hand grip and of the thigh muscles. Some patients were given an initial dose of 50 mg., while others received 20 mg. Additional curare was injected at intervals of two to four minutes until the desired effect was produced. The largest dose given was 100 mg. Eight patients showed increases in range of motion while under the effect of curare, while 9 showed no essential change. The test should be of practical importance

in establishing the correct approach to therapy. In 5 of 7 patients with fracture who showed increase in range of motion from curare the improvement was retained in full or in part, an observation which suggests the possibility of using curare as an adjunct to treatment in such cases. Curare can relieve joint pain by relaxation of muscular spasm.

J. A. M. A.

INTRANEURAL TOPOGRAPHY OF THE RADIAL, MEDIAL AND ULNAR NERVES. SYDNEY SUNDERLAND, Brain **68**:243, 1945.

Sunderland studied the arrangement of fibers within the nerve trunks of the radial, medial and ulnar nerves. Adult human radial, medial and ulnar nerves were dissected for their entire lengths and studied histologically in serial sections. The arm of a full term fetus was also studied in serial sections. Additional human nerves were studied by microdissection. The number of funiculi was found to vary widely in the same nerve at the same level in different specimens. Funiculi also varied widely in size. There was no constant tendency of funiculi to multiply in the neighborhood of the site of branching or to fuse at points between branching. In the radial nerve the number of funiculi decreased distally. In the medial and ulnar nerves the number was greatest distally. The size of the funiculi and their number were found to be inversely related.

Sunderland found that the funicular pattern was continually modified along the entire length of the nerve by the repeated division, anastomosis and migration of the nerve bundles. The average length over which the pattern remained constant was 0.25 to 5 mm. Funicular intercommunications were of three fundamental types: (*a*) division and fusion of funiculi within a compact localized group of bundles, the constituent fibers of which were derived entirely from one branch; (*b*) anastomosis of the constituents of one bundle group with the adjacent bundles of another; (*c*) bundles of fibers of different branches which had intermingled at distal levels. The dispersal of fibers occasioned by the intercommunications was effected gradually. Despite the changing plexiform character of the funicular pattern, fibers from peripheral branches pursue a localized course in the nerve for variable, though often considerable, distances. Sunderland discusses the significance of these intraneural relationships to the effects of nerve injury and regeneration.

FORSTER, Philadelphia.

THE SYNDROME OF PYRAMIDAL IRRITATION: AN ATTEMPT AT HIERARCHIAL CLASSIFICATION OF CLINICAL SIGNS. G. A. MANCEAUX, J. ROBERT D'ESHOUGES and M. JORDA, Encéphale **38**:460, 1949.

One of the most valuable signs of a pyramidal lesion is the dissociation of a decreased or an abolished cutaneous reflex and the exaggerated tendon or bone reflex. The cutaneous reflexes are under cortical control by way of the pyramidal tracts. The tendon reflexes are under the control of the red nucleus by way of the rubrospinal tract. This subcortical system is physiologically inhibited by the higher, corticopyramidal system. Thus the absence of cutaneous reflexes is a direct, negative sign, whereas the increase in tendon reflexes is an indirect, positive sign, which betrays the liberation of lower centers.

Believing that their French colleagues are not sufficiently aware of the importance and value of the different elements of the syndrome of pyramidal irritation, the authors emphasize, recall and reclassify such signs. They divide the signs into three groups—those at the level of the superior member, the inferior member and the face.

Thus, for the lower limb they discuss the reflexes of Babinski, Mendel and Bechterew, Rossolimo, and Gonda; the tibiofemoral reflex of Guillain and Barre; the posterior peroneofemoral reflex; the adductor sign of Sternberg, and others. For the upper limb, they discuss the biceps, radial, triceps and cubitopronator reflexes, as well as the Hoffmann, Starling, Lesny-Vitek and Leri signs. At the level of the face, they rely on the masseter reflex (jaw reflex) and the "cranial" reflex (reflex of the frontal aponeurosis). The article is a brief review of the commonly sought reflex signs, many of which have only doubtful value as compared with those which are considered standard for eliciting evidence of pyramidal involvement.

ZINKIN, New York.

RELATION OF BLOOD SUGAR TO ANTICONVULSANT THERAPY. PAULO DA SILVA LACAZ, An. Inst. de psiquiat. 1943, p. 63.

Both electric shock and metrazol® convulsions were followed by hyperglycemia, which was never of high enough degree to cause glycosuria. After metrazol,® the average rise in blood sugar for 10 patients following induced convulsions was + 52 mg. per hundred cubic centimeters above the initial reading after fifteen minutes, the amount rising from 75 to 114.3 mg. per hundred cubic centimeters. After sixty minutes, the average blood sugar was 73.6 mg. per hundred cubic centimeters. For 15 patients with induced electric shock convulsions, the blood sugar fifteen minutes after convulsions was + 42 mg. and sixty minutes later + 6 mg., per hundred cubic centimeters. The average initial blood sugar level was 95 mg., rising to 135 mg. in fifteen minutes and coming down to 101 mg. in sixty minutes. The hyperglycemia after electric shock was somewhat more persistent. The blood sugar after electric shock also rises more precipitously. The ratio, $\left(\frac{M}{I}\right)$, of the average maximal figures for blood sugar and the average initial reading was 1.5 for metrazol® and 1.42 for electric shock. In 5 cases studies on the blood sugar were made after injections of metrazol® which did not result in convulsions. The average initial blood sugar level in this series was 69.8 mg., and after thirty minutes, 70.6 mg., per hundred cubic centimeters. The variation in blood sugar was within normal limits and corresponded to normal oscillations discussed by Hansen. The blood sugar dropped to maximal low values four hours after insulin treatment. After the first few days of treatment, the author noted that hyperglycemia followed maximal hypoglycemia even prior to the administration of dextrose. This rise in blood sugar was noted three to four hours after the initial injection. In 1 patient the blood sugar rose when a convulsant dose of metrazol® was injected during hypoglycemic insulin coma.

N. SAVITSKY, New York.

Diseases of the Brain

ORIGIN OF THIRST IN DIABETES INSIPIDUS. J. H. HOLMES and M. I. GREGERSEN, Am. J. Med. **4**:503 (April) 1948.

Holmes and Gregersen studied 5 cases of diabetes insipidus in order to evaluate the mechanism of polydipsia under the following conditions: (1) intake of water ad libitum, (2) beta-hypophamine (pitressin®) therapy, (3) forcing of fluids and (4) ingestion of salt. During intense thirst there was a reduction in salivary flow. When thirst was abolished by pitressin® therapy or by the forcing of fluids, the salivary flow increased to normal values. These observations are consistent with the "dry mouth" theory of thirst. Pitressin® therapy or the forcing of fluids resulted in an increase in plasma volume and extracellular volume over the values observed for untreated diabetes insipidus. The thirst mechanism in diabetes

insipidus is similar to that observed in simple dehydration and is caused in this instance by the severe polyuria. This hypothesis is confirmed by the observations that pitressin® therapy or the forcing of fluids alleviates thirst and produces increases in plasma and extracellular volume and in salivary flow similar to those observed after ingestion of water in dehydration. Salt, while it may be effective in maintaining plasma volume and available fluid at the same levels as those observed under pitressin® therapy and when fluids are forced, does not abolish the thirst of diabetes insipidus; on the contrary, it increases the polydipsia. The reaction to salt is the same as that seen in the normal person.

J. A. M. A.

Abnormal Innervation of the Sphincter Pupillae and Ciliary Muscle Following Third-Nerve Regeneration. W. Ritchie Russell and M. Hatfield Wright, J. Neurol. Neurosurg. & Psychiat. **11**:288 (Nov.) 1948.

Russell and Wright report the case of a bombardier aged 29 in whom a head injury was followed by an ocular palsy of the left eye. There were ptosis; dilated, fixed pupil, and loss of all movements of the left eyeball. When reexamined ten months later, the patient complained of visual difficulty, apparently related to paralysis of accommodation in the left eye, while the right eye "had never been strong." At this time there were absence of reaction to light in the left pupil and defective upward and downward movement of the left eye; and, while movement to the left and right was good, on his looking to the right, a marked contraction of the left pupil occurred. The same phenomenon occurred on convergence. In this not only the sphincter pupillae but also the ciliary muscle was made to contract. When this occurred, near vision, which had been reduced to his reading Jaeger type 12, was improved to his reading Jaeger type 1. The authors interpret these findings as evidence of abnormal regeneration of the oculomotor nerve, resulting in mass innervation of the muscles supplied by it.

N. Malamud, San Francisco.

A Case of Cerebral Amoebic Abscess Treated by Modern Chemotherapy. E. A. Turner, J. Neurol., Neurosurg. & Psychiat. **11**:291 (Nov.) 1948.

Turner reports the case of a soldier aged 20 who, while serving in India, exhibited signs of abscesses of the brain. There were also pulmonary signs and papular lesions in the skin. The illness lasted four and one-half months and terminated fatally. Autopsy revealed multiple cerebral abscesses on the left side, diffuse meningoencephalitis, unresolved pneumonia and pulmonary abscesses. In the opinion of the author, the primary focus may have been the pulmonary abscesses. Treatment consisted in repeated decompression and aspiration of the abscesses and of chemotherapy, including use of penicillin, sulfonamides, streptomycin and, finally, emetine hydrochloride. Administration of emetine was begun only three months after the onset, when, for the first time, Entameba histolytica was demonstrated in a smear from the abscess pus. The usually long period of survival in a case of amebic abscess suggests that if modern chemotherapy had been given earlier a cure might have been obtained. The author emphasizes the importance of examination for protozoa in areas where E. histolytica is endemic, early radical surgical intervention and use of emetine and antipyogenic chemotherapy.

N. Malamud, San Francisco.

MENINGIOMA OF THE SPHENOID RIDGE IN A CHILD. COLLIN S. MACCARTHY and LOUIS J. GOGELA, J. Neurosurg. **2**:182 (March) 1949.

MacCarthy and Gogela report the case of a 12 year old boy with a meningioma of the sphenoid ridge. They believe that the patient is the youngest whose case is on record. Proptosis of the left eye was first noted at the age of 5 years. The tumor was asymptomatic until three months before the patient's admission to the hospital, at the age of 12, when he complained of headache, especially severe about the left eye and radiating to the occipital region. The pain progressed in frequency and severity and was accompanied with nausea and vomiting ten days before his examination. There was protrusion of the left eye with some downward and outward displacement. Visual acuity was decreased to 6/30 in this eye. Roentgenograms of the skull revealed a large mass in the left frontoethmoid region which had eroded the supraorbital ridge, the roof of the orbit and the greater wing of the sphenoid bone. There was a diffuse opacity of all the paranasal sinuses.

At operation a psammomatous meningioma was found attached to the periosteum of the orbital roof and the crista galli. It had involved the greater wing of the sphenoid bone, the crista galli, the orbital plate and the posterior wall of the frontal sinus. The tumor was removed entirely.

Six months later the patient had had no return of his headaches, nausea or vomiting. There were no convulsions. No motor or sensory disturbances were found. There was slight persistence of a downward and forward displacement of the left globe, but the ocular movements, the fundi and the visual fields were normal.

TOZER, Philadelphia.

TEMPORAL ARTERITIS. L. JUSTIN-BESANÇON, H. P. KLOTZ, A. RUBENS-DUVAL and H. SIKORAV, Semaine d. hôp. de Paris **24**:863 (March) 1948.

Justin-Besançon and his co-workers report a case of temporal arteritis in a woman aged 70. The disease is rare in France. The patient presented a temporal and a general syndrome. There were definite signs of inflammation of the two temporal arteries. They were increased in size, and there were swelling and redness of the skin overlying the arteries. Palpation revealed considerable tenderness and hypertrophy of the two temporal trunks, which were hard, pulseless and thrombosed. Some segments of the occipital arteries and of the left facial artery presented an identical picture. All the other branches of the arterial tree appeared normal. The patient suffered severe headaches, particularly in the temporal, occipital and nuchal regions. She was pale, and her face had an anxious expression because of the intense pain. The temperature varied from 100.4 to 101.4 F. A portion of the left temporal artery was excised. Microscopic examination revealed subacute arteritis obliterans, with a focus of fibrinoid necrosis and macrophagic giant cell granuloma. Pain was alleviated considerably. The fever did not subside in spite of the arteriectomy. Penicillin proved ineffective. Sixty-four grams of sulfadiazine was administered within eight days; the temperature was restored to normal; pain and swelling disappeared almost completely, but the absence of pulsation persisted. A follow-up of seven weeks is too short a period in which to decide whether a definite recovery or a remission had occurred. Temporal arteritis is a clinical, anatomic and pathologic entity. Despite the diffuse character of the syndrome, the term temporal arteritis should be retained to emphasize the major symptom and to facilitate the diagnosis.

J. A. M. A.

TUMOR IN REGION OF THIRD VENTRICLE: ELECTROENCEPHALOGRAPHIC DIAGNOSIS. P. W. LONGO, P. P. PUPO, A. M. PIMENTA and O. LEMMI, Arch. de neuro-psiquiat. **6**:169 (June) 1948.

The authors report a case in which electroencephalography was of help in making the diagnosis of a tumor of the third ventricle. A white woman aged 36 was admitted to the hospital with a history of severe paroxysmal headaches for four months, accompanied with vomiting, diplopia and recent progressive diminution of vision. Shortly before admission, there were attacks of loss of consciousness. Neurologic examination showed left hemiparesis with hyperreflexia but no Babinski sign, unilateral paresis of the sixth nerve and bilateral papilledema. There was some clouding of the sensorium. Examination of the spinal fluid disclosed an initial pressure of 35 mm. on suboccipital puncture in the lateral position and a final pressure of 0 after the removal of 10 cc.; the fluid was clear, with a few cells. The Wassermann reaction was negative. A roentgenogram of the skull showed no changes in the sellar region. Iodoventriculography showed changes suggesting a tumor of the third ventricle.

Alpha waves were present in both hemispheres, especially the right, and particularly in the central and frontal areas. Six per second waves, called theta rhythm by Walter, with an average potential of about 80 to 90 microvolts, were symmetric in the two hemispheres and were more evident in the central and frontal areas. The presence of these theta waves suggested a deep-seated midline tumor, probably in the diencephalon. The presence of delta waves with phase reversal, predominantly in the right frontal region, was interpreted as indicating extension of the tumor into the right frontal lobe. At operation a cystic, pedunculated tumor arising from the region of the sella turcica and invading the third ventricle and right frontal lobe was found. The histologic diagnosis was a tumor of Rathke's pouch.

N. SAVITSKY, New York.

THE CEREBRAL CAROTID SINUS SYNDROME. E. MØLLER and I. OSTENFELD, Acta psychiat. et neurol. **24**:59, 1949.

Møller and Ostenfeld report the case of a man aged 37 with a history of unilateral headache and nervousness which subsided with the development of a carotid sinus syndrome. The chief features of an attack of the syndrome were lowering of the level of consciousness and slowing, hesitancy and, finally, cessation of speech. A visual phenomenon of "things being distant" and of the "ceiling rising" also occurred. The patient could comprehend what was said to him, and after an attack he could reproduce it. During an attack he felt helpless and stared ahead; his pulse was about 60 per minute, and his pupils were enlarged. Although he was able to stand, he felt weak. The attack was climaxed by a loud, compulsive crying spell, as he began to recover his normal state. The attacks either were spontaneous or could be induced by physical exertion, such as climbing stairs. About five months after the onset of the illness, other symptoms appeared before an attack. These consisted of paresthesias along the right side of the lower jaw, palpitations, a sensation of tightening along the carotid arteries and a feeling of suffocation. During an attack jerking movements appeared in the left leg. The right side of the neck became tender to palpation, and extrasystoles were noted. Attacks simulating the spontaneous ones could be elicited by pressure on the carotid sinus, ascending stairs, hyperventilation and administration of nicotinic acid subcutaneously or of amphetamine sulfate intravenously. A tumor, the size of a tangerine, was finally detected on palpation and removed surgically. The mass had apparently displaced the right carotid artery. Pathologically, aberrant thyroid

tissue was disclosed. Spontaneous attacks ceased with the operation, but pressure on the carotid sinus would produce a similar attack, associated with jerking of the leg. The authors relate the entire picture to a dysfunction of a center in the midbrain, the symptoms being initiated by the carotid sinus, which was distorted and stimulated pathologically by the tumor.

PISETSKY, New York.

DISSEMINATED SCLEROSIS AND GLIOMA OF THE BRAIN IN THE SAME PATIENT: REPORT OF A CASE. C. J. MUNCH-PETERSEN, Acta psychiat. et neurol. **24**:599, 1949.

Munch-Petersen claims that in his experience the coincidence of glioma and disseminated sclerosis is rare. He describes the case of a woman aged 49 who had a bout of "influenza" in April 1939. Two weeks after the onset of the illness she complained of transitory tingling paresthesias and slight weakness of the right arm and leg. Six months later she complained of giddiness. Six years later there occurred sudden paralysis of the left arm, which persisted two or three months, followed gradually by weakness of both legs and a reeling gait. Neurologic examination revealed normal cranial nerves, and the upper extremities presented no abnormalities. The abdominal reflexes were absent. There were slight ataxia and spasticity of both legs with a bilateral Babinski sign. Examination of the spinal fluid revealed 14 lymphocytes per cubic centimeter and a total protein content of 60 mg. per hundred cubic centimeters. The test exhibited a curve resembling that of dementia paralytica. The patient was treated with neoarsphenamine U. S. P., blood transfusions and exercises for gait and coordination. Her condition improved, and she was able to do her housework until more than two years later, when she complained of fatigue and suddenly lapsed into unconsciousness. Examination disclosed incipient papilledema, slight spontaneous movements of the limbs and a Babinski sign bilaterally. She died without regaining consciousness. Autopsy revealed a tumor the size of an orange in the left hemisphere, extending from the external capsule caudally into the mesencephalon and pons. There were recent hemorrhages in the tumor. Examination also showed numerous small, disseminated patches, many near the walls of the ventricles. There was also a patch of demyelination in the posterior columns of the spinal cord. Microscopic examination showed a demarcation between tumor tissue and the brain. The cells of the tumor contained little cytoplasm and were surrounded by fibrils forming a dense syncytium. A diagnosis of ependymoma was made. In sections stained for myelin sheaths the patches were not sharply defined. The axis-cylinders in the patches had almost completely disappeared, with little glial reaction. The author considers this picture rather atypical.

PISETSKY, New York.

Diseases of the Spinal Cord

DISSECTING ANEURYSM OF AORTA WITH HEMORRHAGIC INFARCTION OF THE SPINAL CORD AND COMPLETE PARAPLEGIA. R. W. SCOTT and S. M. SANCETTA, Am. Heart J. **38**:747 (Nov.) 1949.

In 698 recorded cases of dissecting aortic aneurysm, the authors found only 3 in which the spinal cord was shown to have been the seat of ischemic necrosis and hemorrhagic infarction. This paper deals with the clinical and necropsy observations in such a case, which exhibited a feature not hitherto observed, namely, a spinal subarachnoid hemorrhage.

Neurologic complications of dissecting aneurysm of the aorta are by no means uncommon. The actual incidence, however, is difficult to determine and varies in

different series. In their survey of the literature, the authors found a total of 28 well authenticated instances of paraplegia and paraparesis, an incidence of 6.6 per cent of definite neurologic complications. Of these, 10 represented ischemia of the spinal cord, 11 ischemic neuropathy and 3 a combination of these factors; in 4 the condition could not be determined. The disparity between the number of patients showing signs of ischemia of the spinal cord and those resulting in paraplegia lies in the fact that there is probably a gross quantitative relation between the number of intercostal and lumbar segmental arteries interrupted and the degree of disability resulting. In the case of dissecting aneurysm of the aorta here presented all the intercostal arteries were severed, causing hemorrhagic infarction of the spinal cord with complete motor and sensory paraplegia.

A clear spinal fluid on puncture has been considered a differential diagnostic criterion favoring the diagnosis of dissecting aneurysm. In this case there was a bloody spinal fluid and spinal subarachnoid hemorrhage had occurred.

ALPERS, Philadelphia.

ISOLATION OF POLIOMYELITIS VIRUS FROM THROATS OF SYMPTOMLESS CHILDREN. H. A. HOWE and D. BODIAN, Am. J. Hyg. **45**:219 (March) 1947.

An outbreak of poliomyelitis in Baltimore in the summer of 1944 gave Howe and Bodian the opportunity to make observations on the presence of poliomyelitis virus in the throats of persons who had had varying degrees of contact with patients with paralytic poliomyelitis. Poliomyelitis virus was isolated from the throats of 1 of 3 patients with poliomyelitis and from 1 of 6 juvenile family contacts, but not from 5 adult familial, 7 juvenile or 6 adult extrafamilial contacts of these patients. Virus was present in the throats of at least 2 of 28 healthy children from a neighborhood playground. One year later these children were shown to have antibody against the viruses isolated from them.

J. A. M. A.

LABORATORY STUDY OF EPIDEMIOLOGY OF POLIOMYELITIS. F. B. GORDON, F. M. SCHABEL JR., A. E. CASEY and W. I. FISHBEIN, J. Infect. Dis. **82**:294 (May-June) 1948.

Gordon and his associates say that in 1945 an epidemiologic study of poliomyelitis was organized in Chicago under the auspices of the Chicago Department of Health. The method was to make a survey of the neighborhoods of verified cases of paralytic poliomyelitis, during which a certain number of contacts and noncontacts were selected for intensive study. Some results had been reported previously. Pools of daily stool collections from 76 persons were tested by inoculation of 2 monkeys each. Of 23 household contacts, 17 were infected, as evidenced by virus in the stool. The incidence of infection in extrahousehold contacts was 9 of 23, and in noncontacts living in the same neighborhood, 2 of 18. None of 5 persons from nonpoliomyelitis (control) neighborhoods and 1 of 7 unclassified persons were infected. These results are interpreted as indicating that during the period of the epidemic contact with an infected person was the usual source of infection within the groups studied, rather than any general widespread factor in the neighborhood.

J. A. M. A.

ROOT PAIN AND PARAPLEGIA DUE TO PROTRUSIONS OF THORACIC INTERVERTEBRAL DISCS. J. G. LOVE and E. J. KIEFER, J. Neurosurg. **7**: 62 (Jan.) 1950.

Love and Kiefer found that protrusions of intervertebral disks occur in the thoracic region in the ratio of 2 or 3 to 1,000 in the lumbar and cervical regions combined. Of 5,500 operations for protruded intervertebral disks carried out

over a ten year period, 12 protrusions in the thoracic region were found. Over a twenty-six year period (1922 through 1948) 17 cases of protrusions of thoracic disks were encountered. The authors report their findings in these 17 cases.

A history of trauma was found in only 5 cases. The protrusion was midline in 11 cases, midline with some lateralization in 3 cases and lateral in 3 cases. This incidence "accounts for the rather frequent signs referable to the pyramidal tract with all degrees of paraplegia, and the frequency of involvement of bowel and bladder as well as sensory deficits." A definite preoperative diagnosis was made in only 3 cases and a tentative diagnosis in a fourth case. In the 3 cases in which a definite diagnosis was made, routine roentgenograms revealed calcification of the affected disk, and in the fourth case pathologic narrowing of the interspace was noted. Myelograms were made in all but 2 cases. The Queckenstedt test revealed no evidence of block in 9 cases; in 3 it showed partial block, and in 3, complete block. The protein content of the spinal fluid varied from 14 to 400 mg. per hundred cubic centimeters. Laminectomy was performed in all cases, and the protruded portion of the disk was removed in 15 cases. Rhizotomy was performed in 8 cases to facilitate mobilization of the cord. In 2 cases only decompression was performed.

The follow-up study of the 17 cases extended from one month to eleven years. "The results of surgical treatment were brilliant only in those cases in which root pain or cord compression or both were present without gross neurologic deficit." Patients who had considerable compression of the cord prior to operation usually had residual symptoms or signs indicative of irremediable damage to the cord.

ALPERS, Philadelphia.

CRAMP IN CASES OF PROLAPSED INTERVERTEBRAL DISC. LIONEL WOLMAN, J. Neurol., Neurosurg. & Psychiat. **12**:251 (Aug.) 1949.

Wolman investigated the incidence of cramp in 204 patients with sciatica due to prolapsed intervertebral disks who were operated on and followed up from one to seven years after the operation. Cramps occurred in 8 per cent of the patients prior to operation and in 26 per cent after operation. In most cases they occurred at night while the patient was in bed and affected the calf, thigh or foot, singly or in combination. Cramps occurring before operation always began after the onset of the sciatica. The postoperative cramps tended to occur immediately after the operation, gradually becoming less frequent over a period of months to years. No cramps were recorded as occurring more than five years after the operation. Of the 16 patients complaining of cramps before operation, 10 were relieved of this symptom after operation. In two thirds of the patients in whom the operation consisted of division of one or two dorsal roots, 30 per cent had postoperative cramps, as compared with 15 per cent of those not having a sensory root divided. Thus, there was a definite relation between section of the dorsal root and postoperative cramp. Occurrence of cramp was independent of the level of prolapse of the disk, and there was no clear relation between the site of the cramp and the level of the lesion. A large lateral protrusion of the disk seemed to be associated more commonly with the preoperative cramp. There seemed to be no prognostic significance associated with the occurrence of cramp, whether before or after operation.

N. MALAMUD, San Francisco.

EPIDURAL HEMANGIOBLASTOMA. S. BRONFMAN and L. ECTORS, Acta neurol. et psychiat. Belg. **49**:433 (June) 1949.

Bronfman and Ectors report the case of a woman aged 54 who experienced girdle pain and progressive weakness of the lower extremities. Examination showed spastic paraplegia with sensory loss and tenderness to percussion over the fourth and fifth thoracic vertebrae. There was a complete subarachnoid block, and myelographic study showed an obstruction at the sixth thoracic level. Surgical exploration revealed the presence of an epidural hemangioblastoma, the removal of which was followed by complete recession of symptoms.

DEJONG, Ann Arbor, Mich.

Peripheral and Cranial Nerves

PITYRIASIS ROSEA ACCOMPANIED WITH BELL'S PALSY. L. G. JEKEL, Arch. Dermat. & Syph. **61**:118 (Jan.) 1950.

The case reported is that of a 15 year old white girl, who first became ill with a common cold, accompanying which was an unusually severe headache. Three days later a symptomless eruption, typical of pityriasis rosea, appeared. One day later the patient noticed a peculiar feeling in the left side of the face, with inability to smile normally or to close the left eye. There was a disturbance of taste on the left side of the tongue, but no other sensory changes were detected. The patient had no fever, and laboratory tests gave normal results. A diagnosis of complete paralysis of the left facial nerve (Bell's palsy) was made.

Three weeks later the patient had recovered completely and uneventfully from both the eruption and the paralysis.

ALPERS, Philadelphia.

MÉNIÈRE'S SYNDROME. M. ATKINSON, Arch. Otolaryng. **51**:149 (Feb.) 1950.

Atkinson points out that deficiency of nicotinic acid, riboflavin and thiamine is responsible for the symptoms of Ménière's syndrome, which is characterized not only by aural disturbances but by general systemic manifestations as well. He indicates a similarity between the symptoms of deficiency of these various factors and the symptoms occurring in Ménière's syndrome. He suggests also that there may be an element of ascorbic acid deficiency because of the observation that vertigo may occur in scurvy.

ALPERS, Philadelphia.

BULBAR SYNDROME FOLLOWING NON-DIPHTHERITIC THROAT INFECTIONS. D. F. JOHNSON. Bull. Los Angeles Neurol. Soc. **14**:182 (Sept.) 1949.

Two cases were studied in which bulbar symptoms occurred after severe pharyngitis complicated by ulceration and pharyngeal abscess, in which a streptococcus was the only organism demonstrated. This situation is obviously parallel to the complication of pharyngeal paralysis after diphtheritic pharyngitis.

Johnson states there is reason to believe that the transmission of toxins from the throat along the regional nerves is the same in the two infections. In diphtheria, however, the abundant exotoxin oftener results in paralytic phenomena.

In 1 of the cases here reported, an albuminocytologic dissociation was observed in the spinal fluid (Guillain-Barré syndrome). Since this paradoxic phenomenon is also found in some cases of postdiphtheritic paralysis, the comparison of the two conditions is further strengthened. The author also stresses that recovery may be expected with energetic treatment with thiamine.

ALPERS, Philadelphia.

SOME UNUSUAL COMPLICATIONS OF HERPES ZOSTER. C. W. M. WHITTY and A. M. COOKE, J. Neurol., Neurosurg. & Psychiat. **12**:152 (May) 1949.

Whitty and Cooke report 3 cases of herpes zoster complicated by myelitis, in which the following unusual features were presented: In 2 cases there were recurrent attacks in different dermatomes over a period of two to three months. This is regarded as an unusual finding, since the zoster virus is considered to confer lifelong immunity by a single attack. The authors suggest that this is more in keeping with cases of herpes simplex. In the third case a zoster infection was precipitated by trauma to the fifth nerve.

N. MALAMUD, San Francisco.

POLYNEURITIS ASSOCIATED WITH THE USE OF "TAPHOSOTE" (CREOSOTE TANNOPHOSPHATE). R. MATTHYS, Acta neurol. et psychiat. Belg. **49**:113 (Feb.) 1949.

Matthys reports the case of a woman aged 23 in whom there developed extensive polyneuritis, the etiology of which was at first obscure. In an attempt to discover a possible toxic cause, it was found that this woman had been taking, over a period of six months, a large number of tablets of "taphosote" (creosote tannophosphate).

DEJONG, Ann Arbor, Mich.

Treatment, Neurosurgery

SURGICAL TREATMENT OF PSYCHOSES. E. LIEBERT and L. DAVIS, Illinois M. J. **93**:203 (April) 1948.

Liebert and Davis review the results obtained with prefrontal lobotomy in 38 cases. Twenty-five patients were benefited, and of the patients whose condition improved, 12 were discharged from the institution. Thirteen patients showed no improvement. All the patients subjected to prefrontal lobotomy had been ill for many years and presented a severe behavior problem in a mental institution. Untoward effects of the operation, such as incontinence of urine, epileptic seizures and lack of initiative following the operation, must be expected in some cases.

J. A. M. A.

OBSERVATIONS ON ROLE OF PENICILLIN IN TREATMENT OF HAEMOPHILUS INFLUENZAE MENINGITIS. S. Williams, M. J. Australia **1**:463 (April 10) 1948.

Williams says that although strikingly good results have been obtained with a combination of the sulfonamide compounds and immune rabbit serum in treatment of meningitis due to Hemophilus influenzae, the mortality rate of this disease is still over 40 per cent. At the hospital with which Williams is connected, penicillin has recently been added to these therapeutic agents, and it was thought desirable to institute some form of bacteriologic evaluation of its usefulness in this disease. An attempt has been made to relate the penicillin sensitivity of the organism to the concentration of penicillin in the cerebrospinal fluid. Twelve strains of type B H. influenzae showed penicillin sensitivities in the range of 0.5 to 2 units per cubic centimeter. Estimations of penicillin in the cerebrospinal fluid of patients with meningitis due to H. influenzae receiving a daily intrathecal injection of 20,000 units of penicillin show that an inhibitory level for these organisms is maintained only for a period of twelve to eighteen hours. It is suggested that intrathecal

injections of 20,000 units of penicillin, spaced at intervals of twelve hours, could provide an adequate and continuous bacteriostatic concentration in the cerebrospinal fluid and thus form a useful addition to the existing methods of treatment.

J. A. M. A.

THYMECTOMY. A. SICARD and C. DUBOST, J. de chir. **65**:593, 1949.

Sicard and Dubost treated 3 patients with myasthenia gravis, 2 women aged 26 and 34 and a youth aged 18, by removal of the thymus. The authors emphasize the importance of preoperative treatment with neostigmine and atropine. Approach to the thymus was obtained by dividing the sternum transversely at the level of the second intercostal space. This procedure provides for a satisfactory exposure and reduces the risk of opening the pleura. Thymectomy is technically easy and has a favorable prognosis. The 2 women were followed for six and three months, respectively. The general condition of both was excellent. There was an increase in body weight of 15 Kg. (33 pounds) in the first patient and of 6 Kg. (13 pounds) in the second. The third patient was operated on recently. He experienced considerable improvement ten days after the operation. Satisfactory results may be obtained immediately after the intervention in some cases, whereas in others they may appear only after a prolonged postoperative period, during which administration of neostigmine must be continued and reduced progressively. J. A. M. A.

TREATMENT OF INFANTILE PARALYSIS IN THE ACUTE PERIOD. V. SANCHIS OLMOS, Rev. españ. de pediat. **4**:133 (Jan.-Feb.) 1948.

The number of cases of poliomyelitis seen in Spain by the author since 1941 was about 1,000. The author found that muscular spasm was independent of paralysis. It was present in all cases of poliomyelitis. Acute muscular spasm indicated a better prognosis for functional muscular recovery than subacute spasm. Muscular block or pseudoparalysis, alone in antagonistic muscles and in combination with spasm in certain antagonistic muscles, muscular incoordination in either spastic or pseudoparalytic muscles and disturbances of the peripheral structures were frequent. Kenny's treatment was of value. The technics for early and late application of warm compresses, physical therapy, manual correction of muscular deformities and muscular reeducation are described in detail. The treatment, which should be given only by physicians trained in the proper technic, prevents talipes equinus, flexion abduction of muscles, obliquity of the pelvis, scoliosis and certain aponeurotic retractions. Sequelae due to destruction of motor neurons are incurable.

J. A. M. A.

OBSERVATIONS ON STREPTOMYCIN IN TREATMENT OF TUBERCULOUS MENINGITIS. R. DUBOIS, R. LINZ, H. LESCHANOWSKI and OTHERS, Acta clin. belg. **3**:1 (Jan.-Feb) 1948.

Dubois and his co-workers used streptomycin in the treatment of tuberculous meningitis and in acute miliary tuberculosis, beginning November 1946. The authors report on the first 26 patients, who were observed during the first five months. Streptomycin was given intramuscularly and subthecally at the same time. Periods of treatment alternated with periods of rest. The first period of treatment was usually forty-five days. Then followed a rest period of twenty days, then a treatment period of twenty days and another rest period of twenty days; after a third treatment period, of thirty days, therapy was discontinued. Twenty-one of the first

26 patients were still alive at the end of five months, and 19 of them seemed clinically cured and could be discharged to sanatorium care for further convalescence. It appears that the prognosis is the more favorable the earlier treatment is begun.

J. A. M. A.

ROENTGEN TREATMENT OF INTRACRANIAL GLIOMAS. A. ENGESET, Acta radiol. **32**:210 (Sept. 30) 1949.

Engeset says that after Nordentoft's favorable experiences in 1916 roentgen ray treatment was advocated for intracranial gliomas. In 1928 Bailey and co-workers concluded that roentgen therapy of intracranial gliomas should be undertaken only after an attempt has been made to extirpate the tumor, provided it was localized, or after a decompression has been done, in case the tumor could not be localized. Engeset analyzes cases of glioma observed at the University Hospital of Oslo between 1932 and 1946. All the patients were treated with roentgen rays, but the majority were also operated on. In most cases the tumor was removed in part; in some cases only a biopsy specimen was taken. In other cases a palliative operation was performed. The 39 cases in which the histologic diagnosis was verified included 18 of glioblastoma multiforme, 12 of astrocytoma, 4 of medulloblastoma, 2 of oligodendroglioma, 2 of astroblastoma and 1 of ependymoma. A second series, of 7 cases, were of tumors in the third ventricle and the pineal region. The condition was diagnosed pneumographically and treated palliatively by ventriculocisternostomy. A third series comprised cases of cerebellar medulloblastoma. The diagnosis was made clinically, and only roentgen therapy was given, by the method of Sosman. All the patients with glioblastoma multiforme are dead. The average period of survival was nine months. Eight of the 12 patients with astrocytoma are surviving and feel better, although they have some sequelae, such as epilepsy, aphasia, cramps and dementia. Of the 2 patients with astroblastoma, a boy aged 6 years is living and in excellent condition, seventy months after treatment; a woman aged 30 died three years after treatment. Of the 2 women with oligodendroglioma, 1 died four years after treatment, but for six months during this period she was able to work. The other patient became symptom free for almost two years but died of a recurrence. Medulloblastomas have been treated in recent years with roentgen rays only, according to the method of Sosman. The results have been encouraging. One patient with cerebellar medulloblastoma is alive, one hundred and thirty-seven months after treatment. One patient has probable radiation injury of the brain after receiving a total dose of 37,250 r to the left hemisphere. In order to avoid dangerous reactions, small initial doses of roentgen radiation should be given for two weeks. Daily doses as small as 25 r are recommended for the first days, especially when decompressive craniotomy has not been performed.

J. A. M. A.

Diagnostic Methods

ELECTROMYOGRAPHY. P. BAUWENS, Proc. Roy. Soc. Med. **41**:291 (May) 1948.

Nerve and muscle fibers are polarized negatively at the center and positively on the outside. These charges appear to neutralize each other during activity, acting as though the limiting membrane had broken down. The sudden disappearance of localized charges results in a readjustment of the electrical balance in the surrounding structures, virtually constituting an external circuit. These disturbances in a nerve or muscle fiber during the propagation of a zone of electrical activity result in a typical diphasic wave (spike potential) when two electrodes in contact with the fiber are connected to a suitable amplifying apparatus. Within

certain limits in muscle the integrated electrical effects of several fibers manifest themselves by an increase in the amplitude of the wave. The motor unit is the smallest unit entering into activity in the intact animal because the muscle fibers respond simultaneously.

Although the weakest possible voluntary movement entails the excitation of several motor units, the activity is not synchronized, and adjacent units have different frequencies. During maximal exertion a certain rhythm somewhat resembling a beat nevertheless is noted.

Investigations in the clinic are carried out by the use of surface electrodes for cursory or collective effects or by coaxial needle electrodes for more accurate, but more restricted samples. Under resting conditions no electrical activity is detected by either surface electrodes on the skin or needle electrodes inserted into the motor unit.

Increased voluntary exertion first increases the frequency of the diphasic wave, indicating motor unit discharge, and then other motor units come into play asynchronously, and probably of a different frequency. (Synchronized activity in motor units occurs as a result of tendon reflexes and electrical stimulation of nerve trunks and under some pathologic conditions.) Failure to obtain sustained waves on maximal exertion is indicative of inactivity of a large proportion of motor units.

Section of the motor nerve abolishes volitional contraction, but after about three weeks autonomous fibrillations occur, recordable as repetitive rhythmic spikes of short duration and small amplitude. "A medley of [high frequency discharges] may occur in motor neurone diseases, as if progressive destruction of a neurone led to a state of irritability at the myoneural junction of which fasciculation is the clinical expression.

"The repetitive character of both the fasciculation potentials and the fibrillation potentials suggests some relationship. Fasciculation might possibly be a kind of synchronized fibrillation occurring at a time when the terminal arborization of the diseased nerve fibre is still apt to transmit impulses from one myoneural junction to another."

A prolapsed disk or constricting lesion produces electrical activity at rest in the muscles supplied by the root or trunks affected by the pressure. In cases of atrophy and weakness of spinal cord origin there is a tendency to synchronization of activity in those motor units which are still intact. In cases of myopathy there are spikes with narrow bases and of small amplitude but of frequencies (except in advanced cases) which approach those of normal muscle. In cases of congenital amyotony sustained electrical activity occurs simultaneously in antagonistic groups of muscles, even though these appear flaccid. In cases of lesions of the basal ganglia rhythmic surges are obtained.

BERRY, Philadelphia.

FLOCCULATION REACTION OF THE CEREBROSPINAL FLUID. R. DELCOURT and C. MANET, Acta neurol. et psychiat. Belg. **49**:96 (Feb.) 1949.

Delcourt and Manet propose a flocculation test of the cerebrospinal fluid based on the thymol turbidity test of MacLagan. A flocculation is observed which resembles that in the colloidal benzoin test. With an increase in the gamma globulin of the cerebrospinal fluid, there is a first zone change in the test.

DEJONG, Ann Arbor, Mich.

ELECTROENCEPHALOGRAPHIC FINDINGS IN THREE CASES OF SUBACUTE ENCEPHALITIS. J. RADERMECKER, Acta neurol. et psychiat. Belg. **49**:222 (April) 1949.

Radermecker reports the electroencephalographic findings in 3 cases of subacute encephalitis. The paroxysmal complexes and dysrhythmias were proportional to the severity of the clinical condition. The author states that the electroencephalogram has both diagnostic and prognostic value in encephalitis.

DEJONG, Ann Arbor, Mich.

Congenital Anomalies

INTRATHORACIC MENINGOCELE. F. X. BYRON, E. E. ALLING and P. C. SAMSON, J. Thoracic Surg. **18**:279-434 (June) 1949.

Byron and co-workers state that a high percentage of mediastinal tumors that are observed to be uniformly opaque, well defined, rounded or lobulated masses in the posterior mediastinum will prove to be neurofibromas. When there are also bony absorption of adjacent posterior rib ends and the cutaneous manifestations of neurofibromatosis, the diagnosis of mediastinal neurofibroma is usually made. The authors cite 3 cases which indicate that this typical picture may lead one into error. In the first of these cases, when the chest was entered posterolaterally through the bed of the fourth rib, a huge, thin-walled cyst was found. Further dissection revealed the cyst wall to be continuous with the dura through a defect arising as the result of enlargement and coalescence of the intervertebral foramens of the second and third dorsal vertebrae, absorption of the pedicle of the third dorsal vertebra and erosion of the posterolateral aspects of the bodies of the second and third dorsal vertebrae. Through this defect could be seen the spinal cord and, higher in the spinal canal, at about the level of the seventh cervical segment, the inferior aspect of a small intraspinal cyst. The defect was closed by utilizing a portion of the cyst wall or dura as a flap. This was then covered by a free pleural graft and a layer of absorbable gelatin sponge. This patient did well after operation. In the second case no effort was made to remove the meningocele, since it was asymptomatic and in a protected place. In the third case the patient died in the course of the operation, and postmortem examination revealed a tissue-thin meningeal sac projecting extrapleurally through the enlarged intervertebral foramen of the seventh cervical vertebra. The spinal cord was visible through the opened sac.

Reviewing the literature, the authors discuss 5 cases; in 2 of these excision of the sac was performed, and the patients died as a result of empyema and meningitis. The chief diagnostic aid in differentiating meningocele and neurofibroma is the intraspinal injection of opaque medium.

J. A. M. A.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY, AND THE NEW YORK NEUROLOGICAL SOCIETY

Robert B. McGraw, M.D., *Chairman, Section of Neurology and Psychiatry, Presiding*
Combined Meeting, Dec. 14, 1948

Principles Underlying the Projective Technics of Personality Measurement. Dr. Z. A. Piotrowski (by invitation).

The projective personality tests have certain aspects in common. All face the subject with an indefinite and vague situation. It is up to him to make something definite and clear of the test material or with the assignment with which he is confronted. When shown an ink blot, the subject gives a limited number of responses. In reality a very large number of equally plausible, and an even larger number of implausible, responses could be given to the tests. The tests owe their validity to the fact that many divergent reactions are obtained from all the subjects tested, while each individual subject limits his responses to a few and tends to repeat them at each reexamination unless—and this increases the value of the tests—his personality has undergone a significant change. Everything that is definite in the individual subject's response is his own subjective contribution, is "projected" by him and thus is an expression of him. There are a number of projective personality tests. They differ in the degree of validity and in the amount of information which they give about the subject examined. The more indefinite the test material, the less conscious effort is required for responding; and the more difficult it is for the subject to realize what he is disclosing about himself, the more valid and useful is the particular projective test.

It is useful to look on the projective tests as psychologic microscopes. They enable one to detect traits in a rapid and easy manner, whereas it would require much more time and effort to detect the same traits through clinical observation. The limitations reside in the fundamental fact that the tests themselves do not indicate the psychologic significance of the traits discovered by the tests. The examiner must know a great deal of psychology and psychiatry in order to evaluate correctly the significance of the test findings. The oldest and methodologically best developed of these tests is the Rorschach test; next is the thematic apperception test. Other projective technics are free association, the Szondi test, handwriting, free drawings, copying of designs, associations to pictures or cartoons, sentence completion, finger painting and play technics. The greater the amount of manipulation required of the patient, the more does the projective test approach therapy. Thus, play technics are usually used not only as a means of personality appraisal, but as a method of therapy as well. Every projective test can give the correct diagnosis of some patients, with prolonged and careful clinical observations as the criterion of validity. As a rule, the more clearcut a case is clinically, the more likely are the test findings to be significant. By far the best diagnostic aid is provided by the Rorschach test; the other tests are poor seconds. In 90 per cent of all the neuropsychiatric cases a correct diagnosis can be made by means of the Rorschach test. In incipient or borderline cases also this percentage can be obtained, provided both the clinical psychiatrist and the psychologist use their respective diagnostic criteria consistently. At the present stage, the learning of

adequate diagnostic Rorschach criteria is largely a matter of personal experience. For this reason, there are wide differences in the skill with which the tests are employed as diagnostic aids. It is probable that the tests will contribute most to the diagnosis of the early stages of organic cerebral disorders and that the Rorschach test particularly can be developed into a very useful diagnostic aid and a better one than, for example, the encephalogram. A beginning has been made in adapting the test to prognostic problems. The results obtained so far are applicable to special problems of prognosis. Much work remains to be done in this area, which is of great importance to the practicing neuropsychiatrist.

Drawings as Objective Criteria for Neurotic Conflict and Their Change During Psychoanalysis. DR. WALTER S. BOERNSTEIN (by invitation).

As long as psychologists are not aware of the existence of the unconscious, the study of personality cannot be successful. This is why even most gestalt psychologists have contributed little to knowledge of personality. Neither Köhler (Köhler, W.: Gestalt Psychology: An Introduction to New Concepts in Modern Psychology, New York, Liveright Publishing Corporation, 1947) nor Goldstein (Goldstein, K.: Der Aufbau des Organismus, Martinus Nijhoff, The Hague, 1934) so much as mentioned the word "personality." The unconscious—completely denied by Köhler—was to Goldstein "nothing but a certain form of recollection, of memory" (page 216). Goldstein clung, moreover, to the old concepts of "the stimulus" and "the organism" (page 77). (It is significant that Goldstein spoke of the "so-called unconscious" [page 202] as though it were an invention of Freud's. "What appears as the unconscious is nothing," he asserted, "but a former excitation gestalt of the organism" [page 216]. Neither the "excitation gestalt" hypothesis, however, nor the taking over of Rubin's concept of "figure-ground formation" from sense psychology [Rubin, E.: Visuell wahrgenommene Figuren: Studien in psychologischer Analyse, Gyldendalske Boghandel, Copenhagen, 1921] is a tool appropriate to opening the road to the forces of the unconscious.) I have shown that perception is not the mere effect of a "stimulus" on "the organism," but that perception is determined also by the person's psychosomatic "type" (Boernstein, W.: *Nederl. tijdschr. Psychol.* **1**: 331-334, 1933; *J. Gen. Psychol.* **15**: 117-131, 1936), and this includes the dynamics of the unconscious.

It is unconscious activities that reveal the essence of a personality. All projective technics are based on this fact. My intention was to develop a test which would facilitate a rapid diagnosis and prognosis of personality disturbances, using simple materials—a test which would easily demonstrate the disturbances in an objective way, that is, independently of the tester's own interpretations. Two groups of symbols were chosen: (1) two lines of circles and two lines of triangles, all drawn as rapidly as possible to eliminate conscious control as nearly as can be; (2) a tree, a house, a couple. In the second group the patient has complete freedom as to arrangement, time and other conditions. Only eradication is not permitted. All verbalization is noted.

A few weeks before presentation of this paper, I learned that Mr. John N. Buck, chief psychologist at Lynchburg State Colony, Va., had developed what he later called the "house-tree-person" test several years before I developed the two parts of my test at Manhattan State Hospital, in 1944-1945. Buck uses the test for detecting mental deficiency, and his whole approach is different. (Buck, John N.: *Virginia Ment. Hyg. Survey*, vol. 2, no. 12, 1940; The H-T-P, Mimeographed Tentative Manual, Lynchburg State Colony, Lynchburg, Va., 1947; *J. Clin. Psychol.* **4**: 151-159, 1948; Use of the H-T-P in the Diagnosis of Mental Deficiency, read at Conference of County Supervisors of Special Education and Public School

Psychologists, State of Pennnsylvania, Nov. 17, 1948). Rorschach testers, too, use the "house-tree-person" test, but in a more static manner than I do. The circle-triangle part of the test seems particularly useful to uncover rapidly disturbances in the patient's relations to his parents.

[In the first part of this paper, drawings were presented which illustrated the value of the test for purposes of diagnosis and prognosis, while drawings in the second part demonstrated changes during treatment. The full text of the paper will be published elsewhere.]

DISCUSSION ON PAPERS BY DR. BOERNSTEIN AND DR. PIOTROWSKI

DR. LAURETTA BENDER: Dr. Boernstein has given a timely discussion on projective technics in neurology and psychiatry. The use of projective technics is well recognized in the field of psychiatry particularly. However, it is now also apparent that no neurologic examination is complete without psychologic studies, including some one or other of the projective technics. I have had a considerable body of experience, with projective technics, and it is a temptation to talk about my experiences. I shall stress the neurologic problems more than the psychiatric because my experience in neurologic problems may be of specific interest, and I shall speak especially about children because I know more about children. A neurologic examination of a child is a very difficult thing. Dr. Piotrowski stated that the Rorschach test is difficult for children because the problems and functions and standards differ for each age level in developing children. This holds also for a neurologic examination of a child. It is likewise true that one person can hardly accumulate a sufficient body of knowledge for each age level to have a standard for neurologic development or dysfunction in children. Therefore it is important to have some kind of projective technic to help one. Projective technics are useful not only for the reasons mentioned by Dr. Piotrowski, namely, that they may show dysfunction in cerebral function, with cerebral disturbance in development or deterioration or actual organic disorders, but also because projective technics give one an opportunity to understand something specific about the body image problems of the subject. A neurologic examination that does not take into consideration the subject's own reaction to a pathologic condition of the brain and the disturbances that arise from it is not a complete neurologic examination. It is true that I as a physician feel that the best technic is a direct one, in which not only do I see the patient, hear him and feel him, but I also relate to that patient, find out how he can relate to me and feel how he is dealing with the anxiety which arises as a result of his disease and what problems arise in his social situation because of his condition. This is best done in the child-adult relationship by taking the child on your lap and treating him as a mother or father should treat a child. Nevertheless, in addition to such a relationship, it is important to have projective technics which reveal the child's problems in other fields. The Rorschach test, for example, is a way not only of determining whether there is an organic disorder in cerebral function but also of revealing the problem of disturbances in body image interpersonal relationships and anxiety. I think Schilder, and I working with him, were the first to realize that the drawing of the man was essentially a self portrait projected from the inside out, that it displayed the problems that the individual had in the field of body image concepts and that disorders in the drawing of the man represented dysfunctions in the body image concepts. The neurologic examination should extend itself into those projective tests which reveal dysfunction and difficulties in personal relationships, as well as those disturbances due to anxiety which arise from cerebral disease, whether it is revealed in neurologic or in psychologic dysfunction.

I should also like to discuss Dr. Piotrowski's paper and quarrel a little with him about his idea that optic imagery is basic to the projective technics. This is true of the psychologists who prepare and analyze projective technics, but not of the patient who experiences them. Every projective technic gives projections from two points of view, that of the patient and that of the psychologist who analyzes it. The question is what fields the two persons can use. Interestingly, our patients can use almost any sensory area, and we as scientists are limited by the fields which we can use. As I see the concept of projection of the inner life out into the physical world, there is no limitation as to what area of sensory function can be used—not only can be used but is continuously being used by the patient. This is especially clear with respect to children. Those of us who have dealt with children, whether those with neurologic deviations or those who are retarded, psychotic or neurotic or present behavior problems, have long been aware that special activity of the child may be looked on as a projective technic. The activity may be symbolic if little toys or puppets and drama are used as the child analyst uses them. If the child is using raw materials, there may be symbolism, too; but in my opinion it is not the most important factor; the patterning and organization and the repetition of various patterns, such as those shown by Dr. Boernstein in his triangles, are also important. One may also think of the whole body in action; therefore, dances, charades and play acting are projective technics. Without doubt, music may also be used in the same way. Incidentally, one may be an active participant in such activities, or merely an onlooker or a listener, and still apply the concept of projective technics. Dr. Piotrowski rightly mentioned the interpretation of dreams as one of the most important and the earliest of the projective technics. Early in my experience with children I used puppets with Dr. Woltman as an effective projective technic. More recently I have come to use the comics, and I suggest that the comics are a sort of cultural T.A.T. test; if one keeps up with the comics, that is, if one has some understanding of them and the way in which children react to them, they will represent an excellent test. This test I have more or less standardized in my own experience. The comics are a kind of projection at a rather primitive level of all the problems of the developing human body, and children use them freely and discuss them freely. Not only does the functioning of the human being project itself in the material available, but the individual, especially the child, must show action and use every one of his action patterns in his various projective technics; therefore no projective technic is without some kind of an action pattern. The Rorschach test cannot be without action, and the drawing test show action; in drama one uses one's own body, and so on. In my own visual motor gestalt test I have always emphasized the motor and action junction with perception.

The other point, brought out especially by Dr. Boernstein's paper, is that in using these technics one is never without the problem of demonstrating relationships —relationships between people and the world of reality or the physical world. In considering the projective technics, one has not only to think of optic imagery and of various sensory patterns and motor patterns and the need of the individual to integrate these patterns but also to show human relationships and the problems arising out of relationships.

Just a few words about the question of symbolism in Dr. Boernstein's paper. I myself was not convinced of Dr. Boernstein's interpretation of the circles, squares and triangles. I suspect that many of the rest of you also doubted the interpretation. After one has had a great deal of experience, which amounts to interpreting many thousands of circles, trees, houses and human faces, together with the Rorschach test, and hours of clinical experience with the psychoanalysis of a number of

patients, one comes to some kind of knowledge which one cannot put over inside an hour, because one cannot give enough examples. If Dr. Boernstein could have given us many hours and many thousands of examples, we should have become convinced, I am sure; instead, he selected a few obvious instances, which are not altogether convincing. I have had a great deal of experience in the interpretation of symbolism in children's art; so I think Dr. Boernstein's contribution is an important one. The art of children is quite different from that of adults, not only in form and maturation but also in symbolism. This is another area where age must be taken into consideration. Let me give a simple example: The alligator or the snake or objects of that sort are not phallic symbols to children; they represent an aggressive parent, and that aggressive parent is threatening to devour the child. At about puberty the symbolism changes, and for a while the object may be even a living phallus; then it later takes on phallic symbolism—or that of a penetrating organ. The same thing can be said about houses and trees and the symbolism in those objects which are seen in spontaneous art. I never get a tree or a house alone, but always get them in composition, at puberty. Mountain scenes, with snow-capped peaks; setting sun; tunnels; bridges; roads leading into houses; erect trees, etc., express clearly the problems of that age. A large amount of information in these interpretations is specific for the individual, but there is also much of general interest at different age levels and for different kinds of problems. Eventually, I have no doubt that one will build up a considerable amount of knowledge in these fields, for wide application. Meanwhile, in using such work as Dr. Boernstein's, one can accumulate this knowledge.

Dr. Martin Schreiber: We are indebted to Dr. Piotrowski and Dr. Boernstein for bringing to our attention, and thus underscoring for us, these two valuable tests—both particularly useful as checks on subjective clinical observations and impressions. Both have a kind of special value because they approach objectivity, even though neither is truly objective in the rigid, scientific, test tube or manometric sense, since both lean heavily on interpretation.

A word of caution should be expressed at this point. Once the drawings have been produced by the patient, and have been looked at by the examiner, the objective phase of the test is really completed. From that point subjective interpretation by the examiner begins. He apparently uses freely both intuitive and free associations and employs in this fashion his own entire inner conscious and unconscious personal armamentarium. I in no way decry the value of such combined intellectual and feelingful interpretative methods. However, I miss in this test any concrete check on the truth or validity of these interpretations, as they are arrived at by the examiner, other than his own inner feeling of conviction. In this respect this type of interpretation, although similar in certain details, differs crucially from the analogous psychoanalytic interpretations of a detail in a patient's dream. In the psychoanalytic situation the interpretation of the analyst is to a large degree corroborated and checked, not only by the patient's free associations, and by the patient's interpretation independently arrived at, but also by the specific, immediate and subsequent reactions of the patient to the analyst's interpretation. Dr. Bender has, at least in part, answered this objection.

Both these tests seem to present to the patient full opportunity for the externalization, by projection, of those specific internal, intrapsychic, balanced or homostatic forces one calls character. In other words, these drawings are "characteristic" productions of the patient in the fullest, most literal sense of the word. It is in this same sense that I believe a patient sees what he sees, claims he sees or is able to see what he does in the Rorschach plates. It should be made clear at

this point that I am using the term "character" in this context to signify those tendencies in the adult to react in a more or less habitual and specific manner to life's situations. These specific reaction trends represent the final resolution within him, or his ego, of the developmental conflict between the demands of his instincts, on the one hand, and the demands of conscience and reality, on the other. It is the resultant of these intrapsychic forces that I believe one taps and gains insight into with both these tests.

For the past ten years I have employed the Rorschach test with all patients undergoing psychoanalytically oriented psychotherapy. I have used it much as Dr. Boernstein has used the drawing test, not so much as a diagnostic check or aid but, rather, as a corroborative check on deep characterologic changes, as distinguished from superficial, symptomatic improvement or change. I present here a short synopsis of how this procedure was carried out, which has warranted my present conclusions concerning the value of the comparative Rorschach estimation.

A Rorschach estimation was made on each patient within the first week of contact, always after the clinical diagnosis was arrived at, and before the inception of intensive psychotherapy. The Rorschach examination was then repeated at intervals varying from six to eighteen months. In my series of approximately 25 patients studied by Dr. Boernstein and myself, we had a minimum of two and a maximum of six Rorschach tests per patient. It is evident that in using the Rorschach estimation in this way we employed it in close analogy with use of the fluoroscopic and roentgenographic examinations of the chest in controlling the clinical observations of the effectiveness of therapy in the treatment of pulmonary tuberculosis. In most general terms, the detailed review of this series, which has recently been reported by Dr. Piotrowski and me, and which will be more fully discussed at another time, seems to warrant the conclusions of both of us that this method has both great usefulness and validity.

I should like to point out another important use of the Rorschach test in a somewhat different, but related, field. I have found it a powerful tool in teaching clinical psychiatry to third year and postgraduate medical students. Most of you have had personal experience with the convincing effect that attendance at an autopsy carries in driving home the clinical, premortem experience in the particular case. There are few teaching tools that approach this in clarity and power. It has been my experience that the Rorschach test functions somewhat like that, but intra vitam rather than post mortem. When our kraepelinian descriptive and dynamic formulations, which usually have been arrived at mainly by anamnestic and observational methods, are confirmed, corroborated and even repeated, in the identical minutiae of language in the Rorschach report, it is a vital, convincing experience for the student, bringing with it the indispensable qualities of acceptance and conviction. In this respect, it is important that the Rorschach estimate be arrived at independently of the opinion of the clinician.

I hope that Dr. Brown will present some drawings which are pertinent to Dr. Boernstein's presentation. In one of the cases, which we have followed closely for the past eighteen months, the results of the Rorschach test, the drawings and the clinical impressions are in complete accord.

Dr. Fred Brown (by invitation): Dr. Boernstein has made a significant contribution in his relational projective technic. I have been using figure drawings for several years, and when Dr. Boernstein came to me with his technic I began to use it, discovering that it had some advantages over the more static technic proposed by Buck. However, much can be learned from independent drawings concerned with the patient's interpersonal relationships. I have been working

with Dr. Schreiber for the last two years, continuing the work he had been carrying on with Dr. Piotrowski, and I am impressed with the similarity of results which we have obtained independently of each other.

With regard to Dr. Schreiber's cases, we have some interesting findings which lend emphasis to Dr. Boernstein's remarks. Unfortunately, I have no slides for these, but they would probably be a handicap, since I should want to go into much greater detail.

The first case is that of a patient seen eighteen months ago, at which time he was given the Rorschach test and was asked to draw "a person" and, after this, one of the opposite sex. These drawings are not relational; they are done singly. The first shows a female without a face; this lack projects evasiveness and a particular unwillingness to make any commitment with regard to the identity of the person. One psychiatrist to whom I showed the drawings remarked, "This looks like Whistler's mother with her legs spread apart." It is true that the drawing portrays a mixture of idealism with forbidden sensuous cravings, and the halo-like frame over the figure (female idealization was projected in the Rorschach test) carries forward this theme. At the time I did not know it, but this man was a practicing, active homosexualist. His male figure is turned away and also lacks a face. He masks the "unknown man," who represents his sexual goal; and in his strong anal emphasis (a characteristic of homosexual drawings, i. e., the stress placed on buttocks) he shows both compulsive and homosexual traits. The long thin staff which he holds at arm's length projects his anxiety about heterosexuality, whereas the rigidly outstretched arm points to potency problems. I might say in passing that figure drawings should be interpreted with caution and that speculation should be so labeled. Here however, was a patient who was sexually in poor contact; he turned away from people, and there was much confusion with regard to masculinity, toward which he strove but which he could not achieve. When he was seen eighteen months later, a Rorschach test showed what Dr. Piotrowski and Dr. Boernstein stressed in regard to the reappearance of human movement (*M*) in the Rorschach test, as well as improvement in the capacity to establish rapport with people. His drawings at this time are bold and full face; sexuality is emphasized strongly, and he seems to be making an effort to meet sex "head on." In the Rorschach test he saw female genitalia, whereas previously he stressed male genitalia and spoke of a feeling of something penetrating. "I do not know what it is, or what it is penetrating." That was part of his problem —what to penetrate. In the Rorschach test at the time of this report he sees male and female genitalia, and the penetration is quite obvious—a phallus entering a vagina. He still projects in these drawings some of the problems which plague him, and they will remain for a while; but he is approaching a stronger sense of sexual identification, a clearer concept of his own sexual differentiation.

My other set of drawings is interesting because it represents deep analytic therapy with a patient who has been seen five times a week for the last two years. This patient was a woman university student who was engaged in promiscuous polymorphous perverse sexual practices. Her first drawing brings out many paranoid elements. We note its rigidity, the inclusion of extraneous details and the peculiar "soiling" of the face which I have found in such drawings. It may indicate self-destructive trends or a threatened loss of identity. At any rate, detachment is obvious. The Rorschach test showed paranoid schizophrenia, and four weeks later this girl began to hallucinate actively. The second drawing was made eight months later, when the hallucinations had subsided and she was approaching a more stable sexual relationship. This shows a female who is wearing slacks and has her hands extended in a graceful manner. The long

nose and hooklike hands still project aggression and masculine strivings, but the change from before is striking, especially in the loosening of the rigid psychic structure. The patient used this drawing in her Christmas cards last year. I am glad she did not use the other; it would have made a not very merry yuletide season for the people who received them. Eight months later she drew a third woman. We note that there are now hands instead of hooks, the slacks have given way to a skirt and there is even some adornment around the neck. This girl is now accepting her feminine role, is going regularly with one man, has graduated from college and seems to be making a good adjustment.

In conclusion, in using not only the Rorschach test but drawings of houses, trees and people, we are obtaining some interesting results, which will probably be presented in the near future. The use of these projective technics, as well as others, in psychosomatic medicine has been most helpful. Dr. Piotrowski and Dr. Boernstein's statements have been found to hold up exceptionally well in the experience of psychologists in psychiatric hospitals and clinics and in other institutions where personality studies are made. Their observations have considerable value to us in delineating the dynamic psychologic processes of the patient. I should like to emphasize that a knowledge of psychopathology is extremely important in the training of any one who deals with projective technics, so that he will avoid projections of his own personality into the content and be on guard against wild, "intuitive" speculations.

DR. HAROLD G. WOLFF: I cannot understand the meaning of the statement that the psychologists, the analysts and those who worked with the projective technics all supported each other in their observations and inferences concerning a given patient. As I understand it, all worked with a concept based on a common psychopathologic picture. Therefore the inferences would be apt to be the same, since the deductions were made from similarly interpreted symbols, expressed at the bedside, on paper, in dreams or in some act of behavior. Would it not be strange if the inferences were at variance?

DR. WALTER S. BOERNSTEIN: Dr. Bender questions the statement that visual images play an important role in self representation of the personality. That their role is important, however, can be shown from several aspects: 1. Images of any sense can be "sensations" (subjective level) and "projections" (objective level). Images, particularly in the higher sensory fields, can be representative of the individual personality. Dreams and hallucinations furnish good examples. Since the optic sense is the dominant sense in man, visual images are most frequent and important. 2. The personality expresses itself unconsciously not alone through images but also, and particularly, through the motorium. But the motorium and vision are interwoven—from amphibians, in which the melanophores function both as nonstriated muscles and as light receptor organs (Boernstein, W.: *Arch. internat. de pharmacodyn. et de thérap.* **61:** 387-417, 1939), to man. Here, in man, increase in the tone of body muscles gives rise to visual images, just as light acts on the muscle tone, and under appropriate experimental conditions visual perception is undistinguishable from sensations of movement (Boernstein, W.: *J. Gen. Physiol.* **15:** 117-131, 1936). Thus it follows that visual images are important in self representation.

Dr. Bender, if I understood her correctly, is of the opinion that children have not the same symbols as adults. Perhaps one should first define the term "symbol." A symbol is not an arbitrary "as if," based on resemblance of some kind; rather, the symbolizing (concrete) and the symbolized (event, feeling, idea) have a psychophysiologic mechanism in common. For example, the "sweetness" of love is the

sweetness of sugar. In other words, it is the identical experience which characterizes the taste of sugar and the psychologic complex, love. The faculty of symbolization is one of the preconditions for any mental development beyond the level of concreteness (Cassirer, E.: Language and Myth, Translated by S. K. Langer, New York, Harper & Brothers, and later authors. Cassirer stated, ". . . All mental processes fail to grasp reality itself, and in order to represent it . . . they are driven to the use of symbols [page 7]. . . . It is only by symbols that distinctions are not merely made, but fixed in consciousness [page 38]." That abstract ["theoretic," "discursive"] thinking stems from "concrete" experience, from "single perception" [page 89], a fact so much propagandized recently, has also been shown by Cassirer: Verbal conceiving "stems ultimately from . . . the compression of given sense experiences. [page 95].") It follows necessarily that children use the same symbols as adults.

Dr. Bender doubts the value of the circle-triangle test. I can only repeat that this test has proved to be useful in rapid diagnosis, as I demonstrated in my paper. That both parts of the test need a great deal of further study goes without saying.

Dr. Schreiber raises the question of interpretation. Interpretations differ, it is true, with different observers. But many of the essential aspects of the drawings can hardly be misinterpreted: e. g., the couples who stand away from or face each other, a tree with or without roots and foliage, etc., as presented in the slides.

Dr. Brown's demonstrations of his patient's drawings, which show improvement convincingly, confirm further the point I have tried to drive home in my paper.

Dr. Z. A. Piotrowski: Dr. Bender questioned whether I had not overestimated the significance of visual imagery. In reply, I should like to express the belief that the visual sense is the most informative of all senses and that visual imagery seems to contribute most to the organism's preparations for actions in the environment. Moreover, attempts have been made with random sequences of sounds (in the Worcester State Hospital) and with tactual sensations (by myself), and the results have been much less revealing than with the visual stimuli. The human subject seems to be more capable of describing visual imagery and visual sensations than any others. It may be chiefly for this reason that the visual projective tests are superior to nonvisual tests so far as personality investigation is concerned. Second, the matter of symbolism, or, more exactly, of treating the projective test responses as psychoanalysts treat the manifest dream material, has been raised. It can be stated definitely that symbolism fails in differential diagnosis. In the first place, the symbolic treatment of a test performance necessitates picking out certain parts of the test record and does not consider the record as a systematic whole. Now, in parts, test performances of various diagnostic categories can agree. For example, the imagery and symbolism of many subjects with obsessive neuroses are like those of many schizophrenic patients. There is no doubt that certain psychotic patients have an unmistakably specific type of imagery and of symbolic reasoning, but it is equally true that most of the ambulatory psychotic patients do not manifest anything pathognomonic in the symbols they produce during testing. The diagnosis, then, can be made only after a systematic and technical analysis of the quality of the images elicited by the tests, especially the Rorschach. The relation of the shape and visual qulaity of the interpreted area to the form and quality of the percept pertaining to that area is one of the most important diagnostic and prognostic aids. When the percepts fit their respective test areas well, the condition of the patient is much better than when the fit is poor, even though the verbal content of the patient's responses may sound confused.

Finally, Dr. Wolff expressed surprise that I should have been gratified by the frequent agreement between the test findings and the clinical observations. He said that an agreement should be a matter of course, since the psychologists working with the tests and the neuropsychiatrists making their clinical evaluations utilize the same frame of reference, there being but one psychopathologic picture. The answer is that we are not yet quite certain as to the exact psychologic implication of each test reaction. We are pleased with the progress that has been made but are aware of the problems, both psychopathologic, in the theoretic sense, and technical, in terms of test procedures and test formulas, that await a solution. The hope which provides the stimulus in this complicated work is that the projective tests may eventually place both diagnosis and prognosis on a more dependable, and a more objective, experimental basis.

Book Reviews

Die Sektion des Gehirns und Rückenmarks und ihre Hüllen. Second edition. By Prof. Dr. med. Berthold Ostertag. Pp. 47 with 18 figures. Springer-Verlag OHG, Mölkerbastei 5, Vienna I, 1949.

This little booklet contains a detailed account of how to make a postmortem examination of the nervous system. The author is an excellent pathologist who has long had a special interest in the nervous system. A systematic procedure is outlined, and then variants are given and their applicability to special cases is discussed. As the author wisely states, each case must be planned individually. Even the removal of the central nervous organs cannot be left to a technician. In some cases the relations of the various intracranial organs to each other are all important; it is then necessary to inject the brain *in situ* through the carotid arteries. This method preserves the form relations but would be improper for an infectious condition in which it is desired to identify the infectious agent. Even after the removal of the brain, its further handling depends on the individual conditions. In any case, the all too frequent habit of simply immersing the brain in a solution of formaldehyde is inadvisable, since many hours or days elapse before the fixative has penetrated into the interior of the brain; this makes any study of the finer histologic details of the basilar regions imperfect. It is necessary that both the clinician and the pathologist be present at the necropsy and that the examination be planned in all its details before it is begun. These, and many other matters, are discussed in this excellent little booklet, which has evidently proved useful to young pathologists. It contains also much interesting historical information.

PERCIVAL BAILEY.

Trabajos del Instituto Cajal de investigaciones biológicas. Volume XXXVIII. Pp. 231. Tipografia Artistica, Alameda 12, Madrid, 1946.

This volume contains a series of six studies by members of the staff of the Cajal Institute.

The first study, by J. F. Tello, concerns the formation of cranial nerve ganglia and the cephalic mesectoderm of the chicken embryo. The article is illustrated by five beautiful collotype plates. The study was made by the Bielschowsky method in blocks, which shows clearly the earliest differentiations in the placodes and neural crest and their relations to the outlines of the cranial ganglia. The neuroblasts of the ganglia come from the placodes, whether epibranchial or lateral ectodermal. The cells of the neural crest may differentiate into neuroblasts, but their participation in the formation of the cranial ganglia of birds must be very slight. The neural crest disperses its elements within the mesoderm.

Pedro Ramón y Cajal gives a summary of his studies on the brain of batrachians, together with some new findings with the Golgi-Cajal method. It is impossible to give a summary of this summary. One is interested to encounter, in the cerebrum of the frog, such old acquaintances as the cells of Martinotti, the cells of Golgi with short axons and the microglia of Hortega.

There is another study of the development of the acousticofacial ganglion in the chicken embryo by Severino Pérez Modrego. He concludes that it arises from cells emigrated from the anterior portion of the labyrinthine placode. Later it divides into the geniculate and the statoacoustic ganglion. The latter receives additions from the neural tube, and the former, from the neural crest, the rhombencephalon and the second branchial cleft.

There are two studies on the virus of poliomyelitis. Enrique Brañez Cepero has studied the experimental production of carditis in the white mouse, and J. Sanz Ibáñez has shown that the dormouse (Myoxus glis) is susceptible to infection with the SK strain of poliomyelitis virus.

Alfonso Cano Monasterio has made a detailed experimental study of the sexual action of the adrenal cortex and of its intimate relations to the gonads. The anatomic substratum of this sexual action he finds in a series of formations of distinct structure lying between the medulla and the cortex in different mammals. His own observations show that this is a unique zone, called sexual, which is identical with the reticular, and within which are encountered fuchsinophile formations in the cells. The fuchsinophile formation of the reticular zone is ambisexual but has a greater tendency to masculinizing action.

These studies are on the high scientific level we have grown to expect from the Cajal Institute.

PERCIVAL BAILEY.

Critical Studies in Neurology. By F. M. R. Walshe, M.D., F.R.S. Price, $4.50. Pp. 256, with 16 illustrations. Williams & Wilkins Company, Mt. Royal & Guilford Aves., Baltimore 2, 1948.

The author is persuaded that medical literature too rarely displays logical and sustained thought. He states: "It is, perhaps, those scientific notions that we take most readily for granted, and receive upon authority with the greatest assurance, that are most apt to repay examination from time to time, and that upon occasion are found wanting when brought to the touchstone of correspondence with facts. The more abstract such a notion the greater the probability that this will be so. Further, in continued currency, abstract ideas seem to harden so easily into concrete facts, and mental constructs come to pass muster for natural phenomena."

To illustrate these ideas, he reprints six of his own critical papers. The first is a long paper, entitled "The Anatomy and Physiology of Cutaneous Sensibility." It is an excellent summary of recent work and gives the *coup de grace* to Head's epicritic and protopathic theory, which should have died in 1909, after the publication of the paper by Trotter and Davies, but was still viable to some extent even after Weddell's important series of papers published in 1945 to 1948.

The next major subject undertaken is the motor cortex, with its Betz cells and pyramidal tract (chapter II). This is elaborated in the paper entitled "On the Mode of Representation of Movement in the Motor Cortex with Special Reference to 'Convulsions Beginning Unilaterally' (Jackson)," which makes up chapter III. More discussion of this subject is found in chapter IV, the main topic of which is "Discrete Movement." Chapter V is a summary of the role of the pyramidal system in willed movements. These are all most important subjects and are well reviewed. One is surprised, however, to find no reference to the important contributions published in 1944 by the University of Chicago, under the editorship of Paul Bucy—the monograph entitled "The Precentral Motor Cortex."

The last chapter, "The Integration of Medicine," brings the reader back to the ideas expressed in the foreword about the function of criticism in medicine. Certainly, most of the papers written in medical journals should be more critically reviewed by author and editor before publication. After publication, there is room for more critical reviews like those of Walshe in this volume. He is keen, logical and shrewdly cynical, but he tends at times to be on the side of destruction rather than that of helpful construction. He lives up to his "covenant of fidelity." As editor of *Brain*, he wields a powerful, and somewhat wicked, pen.